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Autoimmune CTDs

(Rheumatic diseases)

1-Lupus Erythematosus (LE)
2-Dermatomyositis (DM)
3-Systemic sclerosis (SSc)
4-Sjögren's syndrome (SS)
5-Mixed CTD (MCTD)
6-Raynaud's Phenomenon
7-Others: (*for MD*):
- A-Rheumatoid arthritis
- B-Juvenile Rheumatoid arthritis
- C-Adult-onset Still's disease
- D- Interstitial granulomatous dermatitis
- E-Relapsing polychondritis

8-Autoantibodies Encountered in Patients with Autoimmune Connective Tissue Diseases

By :
DR.Hány Abou-Elwafa
0104018946

Auto-immune connective tissue diseases (AI- CTDs)

Introduction and nomenclature:

The autoimmune connective tissue diseases (AI-CTDs) are a group of polygenic clinical disorders often having heterogeneous and overlapping clinical features; A hallmark of these disorders is the production of circulating autoantibodies (aAb) that have been identified by various immunochemical techniques.

They are called connective tissue diseases because all of them associated with pathological changes in collagen eg.;

*SSC:Associated with collagen hyalinization.

*LE and DM: Both show increased dermal mucin.

*Bullous SLE:Associated with autoantibodies against collagen VII.

The term 'Rheumatic diseases' can be used synonymously for AI-CTD. It should be noted that the older designation, 'collagen vascular diseases', is an obsolete terminology that should be avoided. Furthermore, the unqualified term 'connective tissue diseases' can cause confusion with genetic disorders that involve structural abnormalities of connective tissue, for example Ehlers– Danlos syndrome.

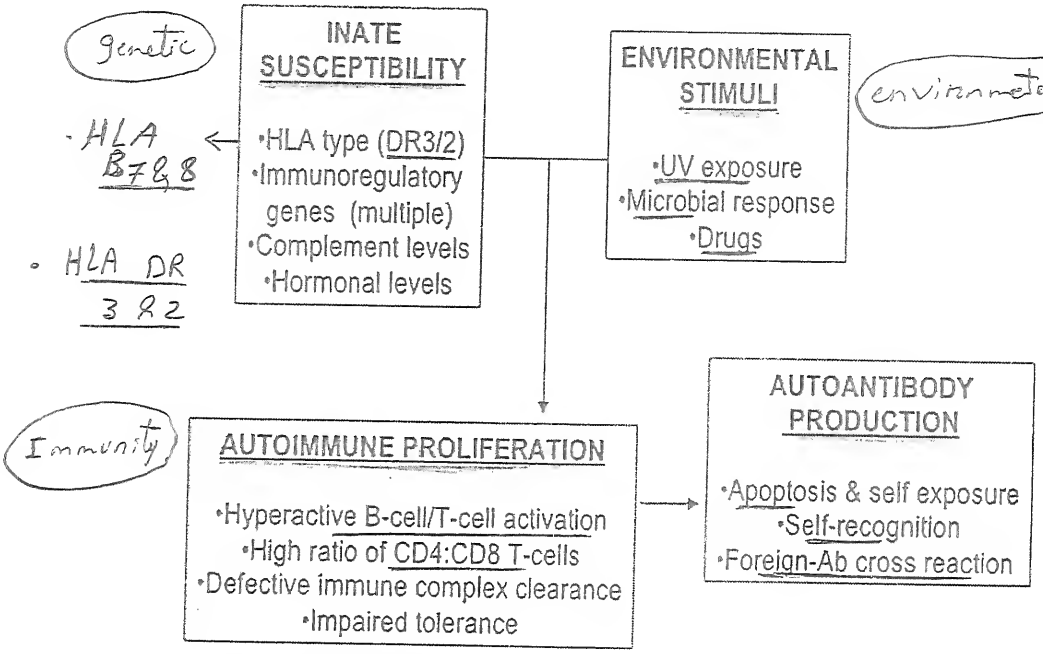
chronic idiopathic AI-CTDs ch' by formation of Auto-Abs against cytoplasmic & nuclear proteins & predominant skin affection

Lupus Erythematosus (LE)

Definition: chronic, idiopathic, AI-CTD with multisystem affection that prominently affects the skin. (ch' by formation of Auts. Abs)

NB: *Lupus means*: any skin disease in which the lesions are characteristically eroded.

Etiology and pathophysiology: uknown (multifactorial): Genetic + Environmental → Autoimmunity (Abs against Cellular Compon. → Cytoplasmic protein, Nucl prote)



In lupus erythematosus (LE), many genetic-susceptibility factors, environmental triggers, antigen-antibody responses, B-cell and T-cell interactions, and immune clearance processes interact to generate and perpetuate autoimmunity

- When LE affects The skin; This is called Cutaneous LE (CLE).
- There are 3 Types of CLE classified According to The degree of dis. progression (& Systemic affects):

- progress in (mos-yrs) → 1 Chronic CLE (CCLE) = Discoid LE (DLE)
- Progress in few wks-mns → 2 Subacute CLE (SCLE).
- Progress in Few days → 3 Acute CLE (ACLE) = SLE. (LE ē Systemic organ involvem.)

NB. Gilliam & Sontheimer Classified the Cut. manifs of LE into:

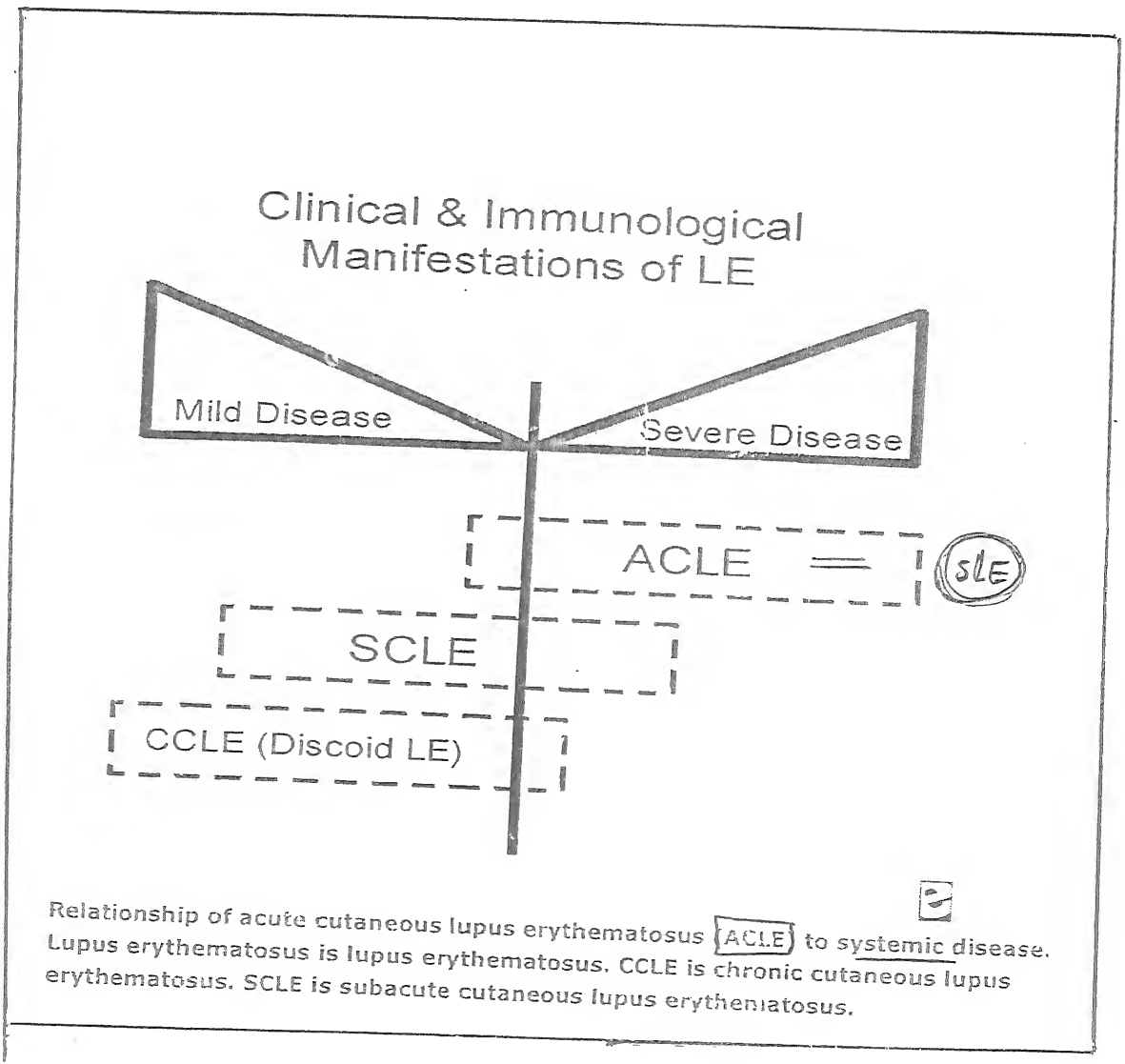
A. Specific: DLE, SCLE & ACLE lesions.

B. Non ~ : ass. ē SLE.

Types of Cut. LE

(Cut. L.E spectrum)

	Chr. Cut. L.E (DLE)	Subacute Cut. LE (SCLE)	ACute Cut. L.E (ACLE = SLE)
• Dis. progression	• Ms - Ys	• Ws - mos	• days.
• M : F	• 1 : 2	• 1 : 3	• 1 : 9
• Cut. lesion	• Chronic Discoid plaques That Heal with (difiguring scars)	• less Chronic, annular or psoriasiform photosensitive Eruption that heal (Confluent-scarring)	• Short lived, Severe Eruption usually Malar rash.
• Risk of systemic affects (SLE) development)	• +	• ++	• (+++) (SLE)
• photosensitivity	• +	(+++)	• ++



Relationship of acute cutaneous lupus erythematosus (ACLE) to systemic disease. Lupus erythematosus is lupus erythematosus. CCLE is chronic cutaneous lupus erythematosus. SCLE is subacute cutaneous lupus erythematosus.

سؤال امتحان

DLE (CCLE)

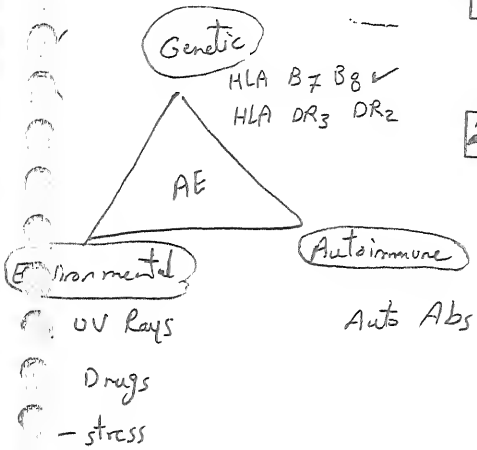
2010

Def. Chr. Benign Cut. form of L.E Spectrum That Chr By

Epidemiology:
- **Age:** any but usually 20–40 y. (Mean 38)
- **Sex:** M:F = 1:2
- **Race:** any but more in (African).
- **HLA-B7 & B8**

Aetiology: → unknown but ± d.t

1. **Genetic:** Exact genetic connect= hasn't been determined (ass HLA B7 & 8). HLA < B7 / B8
2. **Environmental:**



ppF • **precipitating Factors:**
- Spontaneous. (2/3)
- Trauma
  - stress
  - Inf.
- **Drugs:**
  - Griseofulvin, Dapsone (غدي)
  - INH
  - Penicillamine

Furosemide-induced lesions → • **Exacerbating Factors:** Sunlight, Cold, Premenstrual.

CIP: classical DLE lesion chr By:

- **Discoid plaque(s):** (صفائح دائرية)

"Rook"

NO

- Single or Multiple
- Well defined
- Erythematous
- Show well formed adherent scales that Extend into a (patulus) hair follicles ≪ Follicular plugging

→ if this plug is removed → chic Sign (سد فتحة)

Called ≪ Tin tack, Carpet tack or Cat tongue ≫

• Healing of the lesion:

يبدأ يصيب ع جوا
عمرة جدا

3- • Atrophy
4- • Scarring

أول حاجة بتبان

1- • Telangiectasia
2- • Dyspigm = Hypopigm : in ! Center
Hyperpigm : in " periphery.

• Site of the Lesion:

1- Skin : Usually Sunexposed ??

2- MM: Oral : LP or DLE picture or Leuko-plakia
Genital : Vagina, anus
Ocular : → Ectropion.

(4)

3- Hair : → Cicatricial Alopecia.

4- Nail : → Subungual Hyperkeratosis.
red blue plate.
Longit. striae.

Clinical Varieties of DLE (13)

1- Localized : to head & Neck (Cheeks, Nose, Ears, Scalp)

2- Generalized (disseminated) : 1- More persistant.
2- Resistant to ~~tt~~
3- More prone to develop SLE (20%)

4. Similar to SCLE but (E) Scales.

3- Hypertrophic (Verrucous) : Simulating : LP, Wart or Nodular prurigo

4- Atrophic : Marked Atrophic Center simulating (LSA(er) Morphea

5- Annular (LE Gyratus repens) : migratory gyrate annular Erythemas.
SCLE

6- Telangiectatic : Reticulated or Blotchy Telangiectasia (LE Telangiectoides)

7- Rosacea like : Similar to Rosacea but (No) Pustules.
• reddish dots
• diffuse Erythe.

↓
punctate atr
white star.

8. Chilblain LE (Hutchinson)
9. Tumid LE. → dermal
10. LE panniculitis. (L. profundus) → S.C
11. LE profundus Hypertrophicus

(2 syndr) 12. LE/LP overlap synd.
13. Rowell's synd.

14. Erosive palmoplantar (&) ⟷ 16. Bullous DLE. (Exaggerated ↑ vaccular interface dermo-epi = Max Jossef space (VIO) → Dermo epi separation ↓ Bullae)
15. child hood DLE.

- **Chilblain LE: (Hutchinson's)**
  - **def** Chilblain like lesions (Circulatory disturbance) may appear some years after DLE in ≃ (6%) of cases. (but ± occur (out) it)
  - **sex:** F > M
  - **clp:**
    - usually ♀, smoker, living in cold areas
    - **lesion:** chilblain like (red or dusky purpule papules, nodules & plaques) at Cold Exposed areas (Fingers, Toes, Nose, Ear) الأطراف
    - (≃15%) of cases will → SLE.
  - **Path** → as DLE
  - **Lab** → usually +ve Anti Ro & (anti Cardiolipin) داخرة
  - **Rx** → DLE may remit but Chilblain LE persist. Rx ttt

DLE في الغالب بيحصل بعد سنوات ولكنه ممكن يسبقه أو يحدثوا معا

ازاى تفرقه عن Chilblain العادى؟؟
- Telangiectasia at Nail folds

- **Tumid L.E (LE Tumidus):**
  - **def.** dermal form of LE (No epidermal affect).
  - **clp:** plaques on photosensitive areas:

Urticarial like lesions in LE. patients may be:

1. Urticarial Vasculitis
2. Tumid LE

- Erythematous
- Swollen
- brawny سمرة
- Tense
- ± annular
- Clear during winter & ✓ (doesn't) leave pigm. or scars.

→ "urticaria like" (but > 24 hrs)

- Pathology
  1. No epidermal changes (Not as DLE) XX as < Follicular plugging & VID
  2. Marked Patchy Lymphocytic dermal infilt. < Interstitial (superf. & deep) perivascular periappend. — Dense
  3. Mucin deposition. (أقل)

NB (سفوى)
- بعض يعتبرها نوع من DLE والبعض يرفض
- لديه وجود VID في DLE

HL ← Another syn.: papular & nodular Mucinosis of Gold or "Lupus Mucinosis".

(Lp) **Lupus Panniculitis (L. profundus):**

- def: LE affecting mainly S.C.T with little or (No) dermal or DEJ affection
- sex: M:F = 1:4
- Clp. it may occur in ass. (é) DLE (60%) / SLE (or) as an isolated finding
- lesion: Multiple, firm, Movable S.C Nodules (usually) affecting: Face, deltoid area, Trunk, buttocks & Thighs. The overlying skin usually NL but may show Atrophy, DL or poikiloderma → Healing → Cup shapped depressed scar (Lipoatrophy) ← may ulcerate.

site: مكان
- Face
- deltoid
- Buttocks & Thighs.

Skin: Normal / Atrophy / DLE / Poikiloderma

(2)

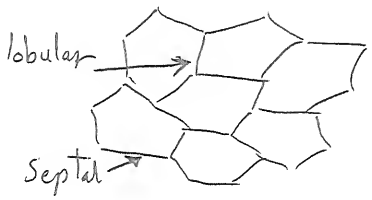
Path. ≪ only S.C.T affection with Little or (NO) dermal or DEJ affect⁻): Salient Histologic Features:

↓ mostly lobular (±) ≺ Mucin / Vasculitis

1. Mostly Lobular panniculitis: ē Lympho-histiocytic infiltrate & ± plasma cells & ± Germinal Center format⁻

May represent Lymphoprolif. dis. related to CTD ϖ has

↓ Indolent Biologic Behaviour.



2. Vascular changes (Vasculitis): ± Lymphocytic Vasculitis

- prominent Endoth
- Thrombosis
- perivascular fibrosis (onion skin appearance)
- Calcificat⁻
- Fibrin deposit⁻ & fat Necrosis → Hyalinizat⁻ of adipose lobules.

3. Mucin deposition.

NB: panniculitis ↑ LP الجلد الدهني تحت : لكلمة ب ناس اختلفوا بتسمية
طبيعي هاد نفضل اسمه LP لكلمة الجلد إلى فوق
L. profundus ← يتبراسمه DLE عليه lesions

NB: 30% show classic DLE lesions.

JB

- L. profundus Hypertrophicus: L. panniculitis with Blackish "warty" skin overlying it.
- LE/LP overlap Synd: Clinically & Histologically bet() LE & LP but (IF) suggest → LP.

H/P ٣ أنواع

- There are ٥ related Conditions:

DLE & dermal
② ← Epidermal Pathology
± Mucin

Tumid LE
③ ← Dermal Path.
+ve Mucin
Patchy infilt

L Profundus
③ ← SC pathology
±ve Mucin
+Vascular Changes ③

Rowell's Synd (EM Like lesions + CLE)

- Criteria for Dx : (Zeitouni 2000, BJD)

A. Major

1. presence of CLE (DLE, SCLE, SLE)
2. EM like lesions (with or without ± MM effect)
3. Speckled pattern of ANA

Target lesion ◎ لوحة النشاء EM

- Annular Erythematous Lesions ē Vesiculo Bullae at Borders
- Acrofacial.
- Exacerbat- by Steroids

B. Minor :

1. Chilblains.
2. Anti Ro or La
3. +ve RF.

- For Diagnosis, 3 Major + 1 minor.

Dx Patient ē L.E who develop EM — How to diff??

- No ppt factors e.g HSV inf.
- Chic Serology of Rowell's < ANA, Anti Ro - La, RF
- ↑↑ Cs & Antimalarial.

- Rowells synd if very severe (may) progress to TEN-like (JAA 2003).

- Pathology ⊙ KC Necrosis
  - ⊙ Focal perivascular lymphocytic infilt. Near the Basal Layer
  - ⊙ dermal Edema

⊙ childhood DLE — الوحيد — M:F = 1:1, FH: +Ve 25%, 50% → SLE

Family History → (25%)

SLE → (50%)

Diagnosis of DLE: (3)

A. Lab: Serology

- 30% → +ve ANA ("low titer" ↓) (Homogeneous > Speckled) ✓
- < 5% → +ve Anti ds DNA, anti Smith, anti Ro [لو إيجابية بتبين إن المريض عنده SLE]
- Chiffelain serology (Anti Ro & anti Cardiolipin)
- Rowell's serology. (ANA, Anti Ro, La, RF)
- +ve RF.
- false +ve serology for ✗.

Others → ↑ESR, Anemia, ↓C, Leukopenia

↑ Serum Ig. ضعف

B. DIF → Lupus band test (LBT) — +ve in lesional (got in sun exp. / 20 in sun protected); -ve in Non lesional.

→ C5b9 test: 60% (+ve) in lesional skin only (at DEJ)

C. Histopathology:

A. Epidermal:

- Hyperkeratosis & Follicular plugging
- Atrophy of St. Malpighii. (3)
- VID & BMZ thickening, Colloid bodies, pigmi incont.

B. Dermal:

- Collagen degeneration (3)
- patchy lymph. infiltr. ✓ Mucin deposit

NB

(1) Relation to SCLE & SLE:

- DLE occur in: ~20% (1/5) → 15-20% of SCLE Cases; 20-30% of SLE
- Progression to SLE: 5% of Adult Cases; 50% of Children Cases.

① disseminated DLE
② chilblain LE
③ childhood

أخطر الأنواع

predic... of pro... to SLE

Type...
- Arthr...
- Anemi...
- Leuke...
- ↑ ESR
- ↑ ANA

- Malignant changes (SCC) may develop specially on top of "hypertrophic lesions".

(2) Does DLE ass. & systemic Manifs?? yes → Arthralgia, Raynauds

Treatment of DLE (D.Daroati) داروتي

Topical

A. General Measures (All cases)

1. Sunprotection program
   - behavioral alteration
   - Sunprotective Clothes
   - Sunscreens > 15 SPF
2. Avoid ppt-& Exacerbating Factors. also Smoking
3. Vit D3

B. Topical Medications:

1- Topical Cs (potent or super potent ē or without ± occlusion)

2- Intralesional Cs: 5-10 mg/ml every 4-6 wks. (غالباً في فروة الرأس scalp)

3- others:
- Calcinurin inhibitors (CIs) (facial lesion)
- Retinoids (Hypertrophic DLE)
- Imiquimod (Anecdotal)
- Cryo.
- IFNα (IL)

Systemic

a. indication:

1- Failed Topical ++

2- Progressive DLE (to SLE)

3- Disseminated ++

→ Antimalarials

Others:
- Cs ✓
- Azathioprine
- MTX
- Cyclosporine
- Thalidomide (نادر)
- Retinoids ✓ ← if Hyper Keratotic
- Dapsone
- Clofazimine
- Vit. E (600 IU)
- β-Carotene (150 IU)
- Danazol
- auranofin

- Other Recent lines (خطوط حديثة)

- Cefaruxine (500 mg/d for 1-5 ms)
- phenytoin.
- Excision.

(٣)

الوقاية

Best ++ (of choice)

Sunprotect + Topicals Cs + Antimalarial

SCLE

• Epidemiology:

- Incidence: 10% of CLE cases
  - ↑ incid. of HLA → DR3 (dr4), DQ1, B8
  - ≥ 50% of cases show ≥ 4 ACR criteria for SLE diagnosis. (mild SLE).
  - 10-15% will → severe SLE
- Age: 15-70 Y/S (average 43 Y.)
- Sex: M : F = 1 : 3 (4)

Clinical picture

1. photosensitivity
2. Cut. Erupt=
3. Mild systemic affects

SCLE lesions

A. Classical SCLE: sudden onset of:
Asymptomatic Non Scarring photosensitive Erupt=: ±

1. Papulosquamous (psoriasiform), (2/3)
2. Annular (Polycyclic) (1/3)

B. SCLE subtypes

1. Drug induced SCLE
2. Neonatal LE (NLE)
3. Complement deficiency Synd. (C2d)
4. Others: oriental & Late onset, Rowells

Mild Systemic

- ≥ 50% show ≥ 4 ACR Criteria of D of SLE But mild form
  - usually arthritis
- Others
  - Alopecia
  - leukopenia
  - DLE (20%)
  - SS.

Clinical Picture & Varieties

Photosensitive Erupt= (BY)

Erythematous Scaly Papules ← evolve into either:
- annular (Polycyclic) (or) Papulosquamous (Psoriasiform)

↳ usually asympt. & has striking onset after sunexposure

psoriasiform
polycyclic

B) ✓ may Resolve with ↔ Telangiectasia / Dyspigmentation (Sp. Hypo or depigm) But (NB Atrophy or Scar) (Central Hypo & peri- Hyp)

. Sites → Sunexposed Areas: [Photosensitive Area]:
- Face (mid facial skin spared but affect the sides)
- Neck
- V-shapped Area of cheat.
- Shawl area (outer upper arms & upper back)

Diagnosis
1- Serology
2- DIF.
3- Histopathology.

Serology & DIF "اهم حاجة"

- 4 +ve
  - Anti Ro (SSA) (80%)
  - Anti La (SSB) (30%)
  - ANAs (80%) [Homogenous]
  - Lupus band test +ve in:
    - 60% of Lesional skin
    - 30% of NL skin. (non Lesional)

Pathology as (DLE) but:-
- Marked: Epid. atrophy
- less Marked:
  - Hyperkeratosis
  - Follicular plugging
  - VID & BM thickening

Drug induced SCLE

a) Drugs:
- Thiazides (Commonest)
- Terbinafine
- Griseofulvin
- Aldactone
- Naproxene
- Diltiazem = [Naloxone / Diltiazem]
- Antihistamines

Q

Neonatal LE (NLE)

(EM 2009)

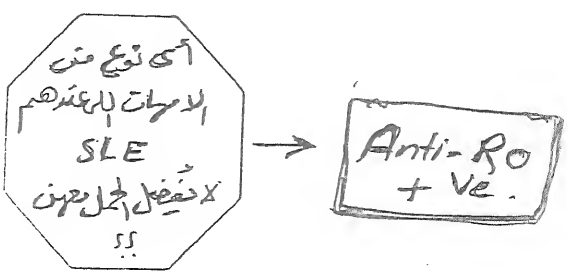
- def. Rare disorder caused by Transplacental passage of Maternal Antibodies & Ch BY: Cardiac, Cutaneous, Hepatic & Hematologic manifs. (2C, 2H)

- Risk Factors:-
  1. Mothers ē HLA B8 or DR3 (SCLE ē)
  2. Mothers ē: +Ve (Anti-Ro, Anti-La & U1RNP)
  3. past History of NLE (↑ incid From 1% → 25!)

- NB: the Mother
  - at time of delivery They are usually NL but (will) develop either defined or undifferentiated
  - → Autoimmune disorder as:
    - SLE or SCLE
    - SS (Sjogren Synd)
    - undifferentiated Autoimmune Synd (AUS)
    - Rheumatoid arthritis. (R.A)

Pathophysiology — See below.

- Epidemiology
  - Age: bet: birth – 1st few ms of life.
  - Sex: (F) slightly > M



Pathophysiology (HL)

The mother produces immunoglobulin G (IgG) autoantibodies against Ro (SSA), La (SSB), and/or U1-ribonucleoprotein (U1-RNP), and they are passively transported across the placenta. The presence of maternal anti-SSA/Ro and anti-SSB/La antibodies increases the risk of bearing infants with neonatal lupus erythematosus. These autoantibodies can be found alone or in combination; however, anti-Ro is present in almost (95%) of patients. Mothers of patients with neonatal lupus erythematosus may have defined or undifferentiated autoimmune disorders, such as systemic lupus erythematosus, Sjögren syndrome (SS), undifferentiated autoimmune syndrome (UAS), or rheumatoid arthritis (RA).

mother → develop (4)

The 52-kd SSA/Ro (Ro52) ribonucleoprotein is an antigenic target strongly linked with the autoimmune response in mothers whose children have neonatal lupus erythematosus and cardiac conduction disturbances, mainly congenital heart block. Anti-SSA/Ro52 autoantibodies recognize the Ro52 protein cardiac 5-HT4 serotoninergic receptor and inhibit serotonin activated L-type calcium currents (ICa). This effect could explain the pathogenesis of the cardiac rhythm disturbances, which lead to an increased risk of diminished cardiac output and the subsequent development of congestive heart failure.[2] However, these conduction defects are caused not only by Ro antibodies but also by anti-SSB/La antibodies and other autoantibodies against cardiac adrenoceptors and muscarinic acetylcholine receptors.

Endomyocardial fibroelastosis

The skin manifestations of neonatal lupus erythematosus occur in the first month or later in life and are mainly due to the presence of anti-SSB/La antibodies, but they may be mediated by other antibodies. Most infants have cardiac and dermatologic manifestations, but some of them may also have hematologic and liver involvement

CIP (4) *

CIP

1. Cardiac (6%) : Cong. HB → 50% Need pacemaker → 20-30% Mortality rate. (also myopathy)
2. Cutaneous (50%) : as SCLE but resolve spont ± leaving (6-12 ms) atrophy, Telangiect. & dyspigm.. (but) no scar. (غالبًا عند البرودة)
3. Hepatic : Hepatobiliary dis.
4. Hematologic (26%) : Sp. Thrombocytopenia ± Neutropenia & Anemia
5. Skeletal:
   - Hydrocephalus
   - Macrocephaly
   - Dysplesia

Note.

Lesions Clically Periorbital → (owl Eye) → Raccoon Sign

(Periorbital → Scalp → arms → legs & Trunk)

"NB ± Small angioma Like" papulonodules.

diseases ← Raccoon Sign?!

100% +ve Anti Ro (also: anti La/SSB, anti U1 RNP)

♀ ✓

Acute Cutaneous L.E (ACLE)

- This Type of Cut. L.E usually ass. with Systemic Involvement So if will be discussed as (SLE).

- def. → يعرف
- Pathophysiology: → يعرف
- Epidemiology: • Age: • in ♀: 14 - 64 Ys (Period of Sex Hormone Product)
  - in ♂: ↘ No predilection. ↓ Age.
- Sex: M:F = 1:9

- This may Explain The role of Sex Hs.
- SLE More Common in Klinefelters.

- CIP: (A.) CIP
  (B.) Criteria For ⊠ (ACR)

A CIP

رشاقة + عرض

	1.	General Manifestations
	2.	Musculoskeletal
2 C	3	Cutaneous
	4.	CNS
2 C	5.	Heart = Cardiac
	6.	Chest
	7	Kidney
	8.	GIT
	9.	OCular
	10.	Hematological

Commonest manifestations of SLE??
1. General
2. Musculoskeletal
3. Cut
4. Kidney

← also the First manifs.

NB:

- 90% < Fever, arthralgia
- 80%: skin (يعني)
- 70%: Renal
- 50%: L.N
- 40%: Pleurisy (Rayn.
- 30% < CNS, Heart

1. General Manifs: (90%)

- Fever (90% ± d.t ← Inf. / Flare of dis / Drugs).
- Fatigue
- L-N
- W.t ← loss: d.t Exhastion from the dis.
  gain: d.t Cs ↑↑ - or N-S

2. Musculoskeletal: (90%)

- Myopathy ē mild Myositis & ↑ serum Aldolase (Not Alk. phosphatase)
- ① Arthritis & Arthralgia: mainly small joints & ± mig. rator. ASYmm. (DD. RA).
- ② deformity:
  - Rhoid like ē S.C. nodule
  - Jacoud Arthropathy.
- ③ AVascular Necrosis of Femur Head: (d.t < dis. ~ Cs)

3. Cut. Manifestations of SLE: (80%) (Acute cut L-E)

* Specific (Show chic Histopath. of LE = VID)

أ-ر ماريات ع (٤)
ARA Criteria

1. Malar Rash
2. Photosenitivity
3. DLE lesions
4. Generalized Morbilliform (Maculopapular) rash on:
   - Extensors: limbs, hands (Spare knuckles)
   - Photosensitive areas.
5. TEN-like SLE (ASAP) [Acute synd. of Para-Epidermolysis]

الترتيب مهم

* Non Specific

1. Vasculitis
2. Vasculopathy
3. Hair
4. Hands
5. Legs
6. others

- Cut. manifs present in 80% of SLE cases
- ~ ~ are the 1st to appear in 25% of SLE cases. Malar Rash أكثر

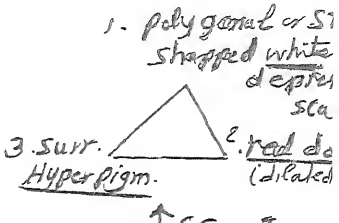
• Non specific Cut. Manifs:-

① Vasculitis:

- LCV (painful, palpable purpura)
- UV. (urticarial Vasculitis)
- PAN like lesions. (Polyarteritis Nodosa).

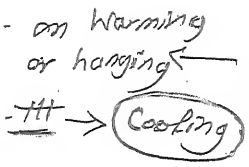
② Vasculopathy:

- Ulcerations
- Livedo Reticularis
- Acrocyanosis
- Degos like lesions
- Atrophie blanche like lesions.



Scare

- Erythromelalgia (Erythramalgia)



③ Hair: Loss in SLE: "cicatricial"

"d.t slow anagen" → cicatricial

- Lupus Hair (Coarse, dry, fragile frontal Hair → unruly appearance with Shortening & Breaking off)
- T.E
- AA. [cicatricial]
- Cic. Alopecia (d.t DLE lesion).

④ Hands:

- periungual Erythema & Telangiect. (Cicatricial) → "ragged cuticle"
- Palmar Erythema
- Raynaud's phenomenon.
- sclerodactly.

CTD

⑤ Legs:

- Ulcers
- Thrombophlebitis.

- Vasculitis
- Vasculopathy

⑥ others.

- L.P
- AN (Acanthosis Nigricans).

- Mucinosis
- symm. Papular eruptn of Extrem.

4. CNS:
- Seizures.
- Psychosis.
- Migrain.
- Hemiparesis.

5. Heart:
- Pancarditis → pericarditis: Commonest cardiac Manif.
- Pancarditis → Myocarditis: Cardiomegally & gallop.
- Pancarditis → Endocarditis: Verrucous
  - Libman Sacks type (non infectious E
  - affect Mitral & Tricuspid (MT)

6. Chest:
- Pleuritis,
- Parenchymal lung dis (More in elderly).

7. Kidney: « Lupus Nephritis »
- Classification Acc. to (ISN): → int. Society of Nephrology
  - Class I: minimal Mesangial
  - Class II: Mesangial prolif.
  - Class III: Focal "
  - Class IV: diffuse "
  - Class V: Membranous
  - Class VI: sclerosing.
- Histopath: chic [Wire loop] d.t Subendothelial deposits of Fibrinoid Material.

8. GIT:
- NVD
- splenomegaly
- Lupus Hepatitis. ✗
- ulcerative colitis.

9. Ocular
- KCs (Kerato Conj. Sicca)
- Corneal Hge & dyspigm
- Retinal Hge.

10. Hematology → See ACR

(B) Criteria For Dx of SLE.

THE AMERICAN COLLEGE OF RHEUMATOLOGY 1982 REVISED CRITERIA FOR CLASSIFICATION OF SYSTEMIC LUPUS ERYTHEMATOSUS	
Criterion	**Definition**
1. Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds & nasal bridge.
2. Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
3. Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation
4. Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by physician
5. Arthritis (2)	Non-erosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling or effusion → ≥2
6. Serositis	a) Pleuritis–convincing history of pleuritic pain, rubbing heard by a physician, or evidence of pleural effusion *OR* b) Pericarditis–documented by ECG, rub or evidence of pericardial effusion
7. Renal disorder (urine Analysis: protein, Casts)	a) Persistent proteinuria greater than 0.5 g/day or greater than 3+ if quantitation not performed *OR* b) Cellular casts–may be red cell, hemoglobin, granular, tubular or mixed
8. Neurologic disorder	a) Seizures–in the absence of offending drugs or known metabolic derangements, e.g. uremia, ketoacidosis or electrolyte imbalance *OR* b) Psychosis–in the absence of offending drugs or known metabolic derangements, e.g. uremia, ketoacidosis or electrolyte imbalance
9. Hematologic disorder (4) (CBC)	a) Hemolytic anemia with reticulocytosis *OR* b) Leukopenia–<4000/mm3 (on two or more occasions). OR c) Lymphopenia–<1500/mm3 (on ≥2occasions) OR d) Thrombocytopenia–< 100 000/mm3 (in the absence of offending drugs).
10. Immunologic disorder (Serology)	a) Anti-ds DNA. *OR* b) Anti-Sm *OR* c) +VE antiphospholipid antibodies *based on:* (1) +ve anticardiolipin (2) +ve anticoagulant; or (3) false- positive serologic test for syphilis (positive for at least 6 months and confirmed by *Treponema pallidum* immobilization or fluorescent treponemal antibody absorption test (FTA-ABS)) [Typical beaded pattern].
11. Antinuclear antibody (ANA)	An abnormal titer of antinuclear antibody by immunofluorescence (or an equivalent assay) at any point in time and in the absence of drugs known to be associated with 'drug-induced lupus' syndrome (>1:160)

cut

syst

NB: ± unilat, Cause di, ± Asym

→ Commonest: Post. Surface Hard Pala

- For diagnosis: ≥ 4 Criteria
- ACR has: Sensitivity : 85%, Specificity : 95%

Some NB on SLE.

1. What is the significance of

- Raynauds → ↓ incid. of Renal affect
- UV → ↑↑ " " "
- Livedo reticularis → CNS affect
- Cut. + CNS affect → Antiphospholipid Antibodies.

UV → Pain Pull
>24 h
Pigm
H/p of vasculitis
ass ē Nephritis

Q 2

Pregnancy & SLE: (Rook)

A Effect of Pregnancy on SLE:

- 1st trimester → Exacerbation (↑↑)
- Next 6ms → improve (↓↓)

after delivery: ↑

- if SLE is in remission 6ms before delivery → pregnancy will pass uncomplicated.

B Effect of SLE on Pregnancy:

dead:
1- Abortion
2- IUFD

live:
3- NLE
4- Live birth (Normal Neonate): (Specially if There is remission on the last 6 ms)

NB

(i). Risk of fetal loss is ↑↑ if: (AP Synd.)

- Abortion
- IUFD

1. History of previous loss.
2. " " Thrombosis.
3. +ve Anti Cardiolipin & Anticoagulant antibodies.

So if:

+ve Anti Cardiolipin & Anticoagulant +

- History of previous loss or Thrombosis → ↓
  - Aspirin +
  - Cs.
- -ve History → No need for ##

Cs in early preg. & in Large doses → Cleft Palate

(ii). Risk of NLE if: +ve Anti-Ro.

C OCPs:

Estrogen containing should be avoided. Safe Methods are IUCD, Mechanical Methods or Progest. only pills.

(Est. ↑ → SLE exacerbation).

D Breast feeding:

allowed if the mother on Cs or Aspirin

Not other Immuno-Supp. XX

3. Types of SLE : (HL) (X)

1- Classical Type

2- Childhood SLE:
- bef. 3-5 Ys
- M:F = 1:4
- More Severe renal & CNS affect

3- Familial:
- rare
- usually ass. with Hypergammaglobulinemia
- Concordance in Monozygotic Twins (70%)
- several other family members have intermittent symptoms as (Synovitis & +ve ANA)

4- SLE of Elderly:
- > 60 Ys
- less incid. of renal & GIT
- ± ass. ē Ss & Lung affect
- +ve Anti Ro & La / HLA D3.

5- ANA -Ve SLE:
- Causes: 1. using non Human substrate
  2. if all ANA directed against ssDNA
  3. SCLE ē photosensitivity (ANA-Ve Anti Ro +ve)
- C/P:
  - Malar rash
  - Photosensitivity
  - oral ulcerat
  - Papulosq. or Annular lesions of SCLE
- Invs: +Ve Anti Ro, anti La & anti ssDNA
  By Time → with ANA +ve.
- Tt: Cs (topical) & Antimalarial.

6- SLE ē genetic C2 deficiency

- AR ck BY SLE + ↓C2 & C4.
- CIP . Cut . marked photosensitivity / marked & severe lesions ē Atrophy . Telangiectasia . scarring .
- CNS & renal affect

7- others: [Rowell's synd. / Oriental SLE.

Q ✓ 8- Drug Induced LE ... ؟ → see ممكد

includes

Drug induced SCLE

- SCLE like clp ē +ve Anti Ro / SSA
- Commonest drug: Hydrochlorothiazides, ACEI
  + E Terbinafin / griseofulvin (others see SCLE)
  + E Naloxone / Diltiazim

Drug induced SLE

4 important Drugs: (5)

HIP - DPM

- H: Hydralazine
- I: INH
- P: Procainamide
- D: D-penicillamin
- M: Minocycl

DNA → Drug induced SCLE → Anti-Ro

Drug induced SLE → Anti Histone

HIP → SLE like picture but ē rare Cut. ↓↓ & renal affection.

- Serology [+ve Anti Histone. / +ve ANA.] (ag)
  -ve Anti dsDNA.
- resolve ē stop of the drug.

DP → - SLE like clp. ē frequent Cut. & ↑↑ renal affection.
- Frequent +ve Anti-ds DNA.

- NB: INH ass ē ≥ 10% risk of renal ✓

• Investigations For L.E

Lab. / Rad. { Joint xR, CxR, CT, MRI, Echo.

Rapid Screening tests (③ reversible)

- CBC
- ESR & CRP
- Urine analysis.

NLE absence of inf

CRP: React more acutely

ESR: Lags behind dis. changes

Both not indicative of dis. Activity

③
- Serum Complement ↓C3 & C4 → Active SLE & LE Nephritis
- Serum Complement ↓C2 & C4 → Complement deficiency Synd. (Czd).
- Serum Gammaglobulins ↑↑

Serum anticoagulants (Lupus Anticoagulants). (30%)

③
- Coomb's Test (+ve).
- Rhoid factor (+ve).
- W-R: False (+ve) for > 6ms. (CFR)

NO Established Criteria For assessment of Progression.

② Test.
- L.E cell Test.
- Lupus Band Test

- Autoantibodies: L.E is an autoimmune disease That's Ch' BY Formation of auto anti_bodies against Soluble Nuclear & Cytoplasmic antigens ω include:-

- ANA
- Anti ds DNA
- Anti Ss DN A
- Anti Sm antibodies.
- Anti_n RNP.
- Anti RO (SS.A) → NLE, Drug Induced SCLE
- Anti La (SS.B).
- Anti phospholipid antibodies.
- Anti Ribosomal.
- Anti histone → drug induced SLE

• L.E Cell Test: (مش بيستعمل لوحده بيتعمل مع AIHA)

. This Test depends on the presence of L.E !? Factor (autoantibody against Nucleoprotein)

• Patients serum (موجود فيه) + NL WBCs ⟶ The L.E factor diffuses into the WBC's Nucleus:

↓ destruction

Nuclear damage & disintegration of Nuclear material

- Phagocytosed by another WBCs (that escape the damage).
  ↓ Wright's stain.
  - Neutrophils ē:
    - Large
    - Rounded
    - Homogenous
    - Basophilic

  Bodies

  Called: L.E Cells

- Surrounded by another WBCs.

  Called: L.E Rosette.

What is
- L.E Cell factor
- LE Cells
- LE Rosette ??

(هتقوى)

. This test ch BY:

↳ Specific Not sensitive.

- +ve in 80% SLE
- +ve in 2% DLE

(مهم) N.B: Not sensitive, +ve in DLE, SSc, RH.A

Lupus Band Test

D.I.F

الأكثر أهمية

It is DIF test to detect IgG, IgM & C3, IgA (Linear or granular) at the Sublamina densa of BMZ (SLD, BV)

← Done By taking Biopsy from both Lesional & Normal skin → Then do DIF test..

	lesional skin	Non lesional sunexposed skin	Non lesional sunprotected skin
DLE	90% +ve	-ve	-ve
SLE	90% +ve	90% (60-100%)	≈ 50% (32-91%) (Sufferarm 7o / buttock 3o)
SCLE	60%	30%	-ve

- Significance:

Differentiation & prognosis

- bet DLE & SLE

① Prognosis of DLE Cases that will progress to SLE (if become +ve in non lesion.

② Prognosis of SLE severity: if it is +ve in sun protected uninvolved skin of SLE cases → Correlates well ⓔ dis. activity, → Hence ⓘ severity of Renal affection.

- +ve Healthy → sun exposed → SLE
  → sunprotected → SLE + Renal

Autoantibodies

• ANA Test (AN Factor).

- ⊙ Very sensitive: (+ve in >99% of SLE Cases).
- ⊙ Not specific: because it is +ve in: [but lower titer]
  - NL individuals (5%)
  - Old age
  - Pregnancy
  - Mg
  - Drugs (Minocycline).

مهم جدا
+ve في الحالات
- SLE: 90%
- SSc: 40-80%

- titer (titre) > 1:160 or (160-320) → Diagnostic
- What is ANA -ve Cases ?? → Non human substrate against SS DNA. SCLE & photosensitivity.

Significance - So this test used as: Screening test to help rule in or rule out SLE Cases.

- Methodology:

Patient's serum (Containing ANA)
+
Substrate: Human Tm Cell line (as Hep-2 cells) (Cultures of Eos. sec)

"Mouse liver ortid. Sections" ←

↘ derived from Human Laryngeal Cell line.

↓ incubation

Add Fluroscent Labelled anti Human γ globulins

(3) Comment on:-
- Substrate
- titer
- pattern.

↓

Comment on (2) things:

- ANA titer
- Pattern of Fluorescence

ANA test (FANA)

Titer

① Higher titer > 1/160 is diagnostic & the higher the titer the more the significance of the dis.

Screening (so used to rule in (or) rule out SLE cases).

- but no relation to dis. activity. progress. duration.

② Higher titer:

- ⓐ present in: SLE. MCTDs. SSc
- ⓑ against ??? DM & PAN

ⓒ Higher Titer in NL individual means → will progress to SLE.

Pattern of Fluroscence

See the table

- Peripheral stain is diagnostic
- other patterns (less common).
  - Homogenous
  - speckled
  - Nucleolar

ANA pattern	Antigen	Diagnosis	prognosis
Peripheral (Membranous)	ⓐ n. DNA (dsDNA)	→ SLE (SSc-Mg)	Poor
Homogenous	Ⓗ Histones	drug induced SLE	Good
	n DNA	→ SLE	Poor
Nucleolar	Nuclear RNA	SSc, SLE	Poor
Centromere	Kinetochore	CREST	Good.
Speckled	Ⓢ M	→ SLE	Poor
	mRNP	MCTD	Good.

- **Anti ds DNA** (Anti native-DNA ; Anti n-DNA)

Specific
Not sensitive (60%)
Asse

- Can be measured by (RIA, ELIZA, IOIF utilizing Crithedia Luciae as a substrate).
- Specific but not sensitive (+ve in (60%) of SLE cases):
- Ass. ē: severe renal affection → Poor Prognosis

peripheral pattern of ANA

- **Anti ss DNA** → not specific: (+ve) in
  - SLE: 60%
  - DLE.
  - MCTD.

- **Anti Sm antibodies**:

Very specific
Not Sensitive

- The (most specific) test for SLE
- Non sensitive (+ve in (20%) of SLE cases)
- Ass. ē ↑↑ incid. of renal & cut. affection →
- More relevant when Anti ds DNA is -ve.

Poor Prognosis

- **Anti nuclear Ribonucleo protein** (nRNP Abs): [U1RNP]

Ch BY

↓

Speakled pattern

- **MCTD** (100%)

↘ Good prognosis

- NLE

Anti La (SS-B)

- +ve in 10% of SLE Cases.
- +ve in 30% of SS & SCLE
- Usually ass. ē Anti-Ro. (See Anti Ro)

Anti RNP are:
- Anti Ro
- Anti La
- Anti U1 RNP.

Anti Ro (SS-A) (Usually ass. ē anti La).

- NLE → 100%
- SCLE → 80%

- SSc/LE overlap → 75%
- Oriental L.E → 60%
- SS → 40%
- SLE → 30%

Anti-Ro + Anti-La.

Anti Histone

Drug induced L.E

NB: 30% of SLE. 50% SSc ✓

"Homogenous" → Homogenous Pattern

good prognosis

Anti-Ribosomal Abs → Lupus Cerebritis.

Antiphospholipid Abs (Anti CL & LA Antibodies)

Cardiolipin
Coagulant

(See APS)

Histopathology of CLE

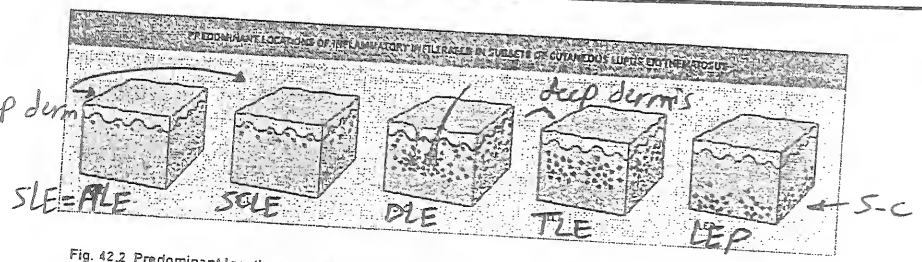


Fig. 42.2 Predominant locations of inflammatory infiltrates in subsets of cutaneous lupus erythematosus. The types of cutaneous lupus erythematosus are: acute cutaneous lupus erythematosus (ACLE); subacute cutaneous lupus erythematosus (SCLE); discoid lupus erythematosus (DLE); lupus erythematosus tumidus (LET); and lupus panniculitis (LEP); the latter three are forms of chronic cutaneous lupus erythematosus. The primary locations of the infiltrates are as follows: superficial dermis, ACLE and SCLE; superficial plus deep dermis and periadnexal, DLE; superficial and deep dermis, LET; and subcutaneous fat, LEP.

Histopathology of CLE

شرح تفصيلي → 1- DLE → Epid, lower & upper dermal (Deeper Pathology)

شبيهان بعرف الـ DLE للتفرقة الظاهرة → [2- SCLE, 3- SLE] → Epid. & upper dermal

1 DLE Pathology:

(A) Epidermal changes: — صفة ثابتة

1. Hyperkeratosis with Follicular plugging
2. Thining (Atrophy) of St. Malpighii
3. VID: Vacuolar degeneration of Basal BCL Cell Layer ass. with — فوق 3
   - BMZ Thickening
   - Dermis: Colloid bodies, Pigment incontenance

(B) Dermal changes: —

1. degenerative Collagen changes: — تحت 3
   - Edema
   - VD
   - RBCs extravasat
   - Collagen Hyalinization
   - Fibrinoid Necrosis
3. Mucin deposit
2. Lymphocytic infilt.: patchy superficial & deep.
   - site ③: periappendageal, Perifollicular, interstitial
   - [also ± lichenoid infilt.]

NB → Rook: For Diagnosis we should have at least 2 of 3:-

1. Vacuolar degen → VID
2. Degenerative Collagen changes
3. Patchy Lymphocytic dermal infilt.

DD of LE

5Ls diseases
- LE (Tumid)
- Light Erupt (PML)
- Lymphocyt'c Infilt. of Jessner
- Lymphocytoma Cutis
- Lymphocytic Lymphoma

clinically & HP] diseases ch by chr. Erythematous Indurated plaques & Patchy der. Infilt. by pathology — 5Ls dise

Tumid LE
- NL Epid
- Marked dermal infilt.

→ Marked Mucin deposits

Jessner
- NL Epid.
- No Mucin Hydropic degen.
- deep dermal & ± SC infilt. (↑B-cells)

PMLE
- upper papillary dermal Edema
- dermal infilt. & some Neutroph
- No Mucin Hydropic degen.

بعض تعبيرهم مرض واحد.

L.E — بعض تعبير

Mucinoses نوع من — Jessner

((5Ls)) إفرضيا

Lymphocytic Lymphoma

&

Pseudolymphoma (Lymphocytoma Cutis).

Both: No epidermal changes.

All → No (NL Epid): + dermal infilt

X
- Hyperk
- Atrophy
- plugging
- VID
- DIF

But — الفرق بينهم

But infilt.

Lymphoma
- bottom Heavy
- Indian Filling (Ext. Cell.)
- Appendageal infilt & destruction

Pseudo
- Top Heavy
- Follicle like aggregates
- Grenz Zone.
- No Appendageal aged infilt. [Germinal Follicles]

Jessner
- Prominent B cells
- CD62-L +ve
- HLA DR-Ve
- T cells.

TLE
- Marked Mucin.

PMLE
- upper papillary dermal Edema
- ± Neutrophilic infilt.

updated EMed. 2010

Treatment of SLE

depends on the severity

- Mild dis e.g
  - fever
  - Cut. manifs.
  - Musculoskeletal manifs.
  - Serositis.

  (Mild)

  → Antimalarial (HCQ) or MTX ± Cs (low dose).

- Moderate dis.
  - Nephritis: mild. Mod.
  - Thrombocytopenia: (20-50 x 10^3)
  - Major Serositis.

  → Induct. therapy ē (MP) (1gm/d for 3ds) then → Maintanence therapy ē (Cs + AZa)

- Severe dis
  - Severe Nephritis. (See Classification)
  - Severe Thrombocytopenia (< 20-000)
  - Severe hemolytic anemia.
  - Lung Hge.
  - Cerebritis.
  - Abd. Vasculitis.

  → Induct ^ th: MP + CYCL (IV) 1gm/m²/d X 7 doses (CYClophc)

  - Complete resp. → maintain ē AZA Cs
  - Partial resp. → Cyclophc 1gm/m² 13ms.
  - No-Respons → Add.: rituxim, IVIG, Calcineu (CIs)

Skin
- Sun protect
- Topical th as in DLE.

- First line of th
  - A Antimalarial
  - C Cs
  - D Dapsone

  (Mild CLE)

HL New Immunomod. (Exhl)
- Leflunamide
- Nucleoside analogues e.g Cytarabine
- rituximab.

Serology of SLE

(9) Antibodies

- ANA → (90%)
- Anti ds DNA (60%)
- Anti Sm (20%)

- Anti-Ro (30%)
- Anti La (10%)
- Anti U1 RNP (nRNP)

- Anti histone (
- Anti ribosomal
- Antiphospholip
(30%

Diagnosis of SLE ✓

(Approach For ⌀)

ANA

- −Ve → Not SLE (or) ANA −Ve SLE
- +Ve → Anti ds DNA
  - +Ve → SLE
  - −Ve → Anti Smith
    - −Ve → not SLE
    - +Ve → SLE

What is the significance of

- ANA: Sensitive.
- Anti ds DNA (Specific) → Severe renal.
- Anti smith (Most ↓) → Severe renal.
- Anti Ro → NLE (100%), SCLE (80%) & ANA −Ve SLE
- Anti-U1RNP → MCTDs (100%) NLE

drug induced

- Antihistone → DILE
- Anti Ribosomal (Lupus cerebritis; CNS affect
- Antiphospholipid → (36)
  (⌀ pregnant)
  - SSC ← Antinucleolar / Anti Centrom
  - ↓ RF ↓ ST

Dermatomyositis

Dermatomyositis (DM): chronic, idiopathic, immune mediated disorder that includes an inflammatory myopathy and characteristic skin manifestations (Muscle+skin affection);

Polymyositis (PM): is an inflammatory myopathy without the cutaneous findings (muscle affection without skin affection).

Etiology: unknown; may be due to: genetic, environmental agents (e.g., virus, drugs) and autoimmunity.

Epidemiology:

* M:F=1:2
* Age: 1.Adulthood type: average 40y 2.Juvenile: 5-14 y.
* Cause of death: Mg, infection, pulmonary and heart affection.

Clinical presentation of DM:

A. Clinical picture:

1. Cutaneous manifestations
2. Muscular manifestations
3. Systemic complications/associations

B. Clinical subtypes (see the table)

C.Criteria for diagnosis.

A. Clinical picture

1. Cutaneous manifestations:

A. Pathognomonic manifestations (2)

1. **Gottron's papules**: violaceous erythematous (Lichenoid) papules overlying the dorsal interphalangeal or metacarpophalangeal, elbow or knee joints.
2. **Gottron's sign:** symmetric, nonscaling, often atrophic violaceous erythematous macules or plaques, in the same distribution as Gottron's papules

Gottron's papules = papules Gottron's sign: Macules or Atrophic plaque (بنفسجي violaceous).

B. Characteristic manifestations (4)

1. **Heliotrope erythema:** violaceous purple erythema/edema at periorbital area (mainly) also cheek, temple and forehead.
2. **Shawl sign/V-sign:** Violaceous Erythema & scaling on shoulder and upper outer arms (Shawl sign) and V-shaped area of anterior neck and chest.
3. **Periungual telangiectasias:** *with ragged cuticle* (dystrophic cuticle).
4. **Mechanic's hand**: hyperkeratosis, scaling and fissring of hands due to ***Gower's sign*** (associated with an increased risk of interstitial lung disease and +Ve antisynthetase).

C. Compatible manifestations (2)

1. **Poikiloderma atrophicans vasculare** (poikilodermatomyositis): violaceous incontrast to that of LE which is erythematous. on Shawl & V shapped areas & buttocks
2. **Calcinosis cutis:** more common in children; firm, whitish/yellowish papules, plaques or nodules on the surface of the skin that may ulcerate and discharge chalky material. Most commonly present on the buttocks, elbows, knees or traumatized areas, *and is associated with increased disease activity and duration.*

D. Less common manifestations (6)

LP.
MG → death
Vasculitis
Panniculitis

- Holster sign violaceous Erythema at Lat thigh.

- Poikiloderma

Erythroderma

Facial swelling

· Scaly scalp (itchy)

Mg + hyperkeratosis

E. Rare manifestations:

3 OSIS (hyperkeratosis, hypertrichosis, mucinosis).

2 urticaria (urticaria and U.vasculitis).

Zebra-like stripes (centripetal flagellate erythema).

* Degos' disease.

2. Muscular manifestations

Common: Symmetrical proximal muscle weakness, difficult walking, getting up from chair, combing one's hair, dysphonia, dysphagia.

Less common: respiratory muscle weakness, visual changes, abdominal pain.

3. Systemic complications/associations

· Heart · GIT · oCWor
· Lung · Kidney · MNgn.

* Heart: Cardiomyopathy.
* Lung: Aspiration pneumonia (secondary to respiratory muscle weakness), Diffuse interstitial pneumonitis/fibrosis
* GIT: Large-bowel infarction (secondary to vasculopathy).
* Muscular: Muscle atrophy and calcification.
* Ocular: including iritis, nystagmus, cotton-wool spots, optic atrophy, conjunctival edema and pseudopolyposis.
* Internal malignancy.
* Renal: Nephritis.

ILD interstitial lung dse

B. Clinical types. (See classification)

(6 Types)

1. Adult DM
   - A. Idiopathic (classical) Type.
   - B. Paraneoplastic Type.
2. Juvenile DM (classical & Amyopathic)
3. Amyopathic DM (DM sine Myositis) & Hypomyopathic DM.
4. Adermatopathic DM.
5. overlap DM.
6. Drug induced ← Hydroxyurea, statins, DP.

1- Adult DM

A Classical (Idiopathic) DM. →

3 ← skin, Ms, Syst

B- Paraneoplastic DM

(DM is one of paraneoplastic syndromes)

- Incid.: 10-25% of DM cases
  - Risk remain ↑ for 3-5 ys after Dx

- Risk Factors:
  1- Adult DM
  2- Women > 45 ys
  3- Amyopathic DM.

Amyopath
o+ > 45y
Mg

- Type of Cancer:
  - Ovarian Cancer
  - Gastric "
  - Colon "
  - Lymphoma.

- Comment:

- less Common:
  - Breast Cancer → Seb Karat
  - Cancer lung
  - ♂ Genital
  - MF.
  - MM (my Melanoma)
  - Kaposi.

So Any Case of DM after age > 45 ys (Sp. Woman)

Follow up by
1- CA.125 (Cancer Ag) → Ovarian Cancer Marker
2- Mammography
3- TV US.
4- Gynecologic Exam.

+

Also: CT
- Chest.
- Abdomen.
- Pelvis.

- others:-
  - PSA (♂)
  - occult Blood in stool
  - Colonoscopy (if appropriate Age, occult Blood in stool - symptoms) Fe def. anemia)
  - upper GIT Endoscopy (if -ve Colonoscopy, ...)

2. Juvenile type: differ from adult type in: (Juvenile 50%) (adult 15%)

* High incidence of calcinosis cutis, GIT complications, low grade fever, arthritis, cardiac conduction defects (RBB) and Gowers sign.

* There does not appear to be any association between juvenile dermatomyositis and malignancy.

XX Mg

3. Amyopathic Type (Dermatomyositis Sine Myositis) (2-10%)

- def: patient with pathognamonic skin changes without clinical (or) Lab. evidence of Muscle involvement for at least 6 (2) years.
- incid. 2-10 % of DM Cases.
- CIP 1- Pathognomonic Cut. changes.

Cut. Signs ē either → or → No Myositis ein 1st 6 ms → later on clinical Myositis. / Subcl. Clinical Myositis MRE

2- Commonly There are: arthralgia, Fatigue, pruritus, Lethargy & photosensitivity. → FLAPP

3- In some Cases: Clinical Myositis develops Later on & in other Cases There is already subclinical Myositis but can be detected by Non-standard Methods as (MRI)

4- ↑ incid of (Mg)

↑ Risk For (Mg)

4. Overlap DM (40%)

- The Patient has Criteria for (+) of DM & other AICTDs as SLE (SSc) SS
- More responsive to (Cs) > Idiopathic DM.

- NB: Hypomyopathic DM :- Skin rash (+) lab (or) Rad. Myositis without clinical Myositis.
  - may or may not → Clinical Myositis.

Skin Rash (+) lab / Radio → Myositis (−) clinical Myositis

5. Adermatopathic : Polymyositis with little or (No) skin affect

others:
- Hypomyopathic DM
- Inclusion Body Myositis

Criteria for diagnosis of DM/PM

A. Bohan Criteria (1977):

5 Criteria for ①④ DM:

① - Typical skin Rash

clinical ② - proximal symm. ms weakness

lab ③ - ↑ ms Enzymes:
- cPK (ypbpc0.1)
- Aldolase
- LDH
- SGot & SGpT

④ · +Ve: EMG

⑤ · +Ve: ms- Biopsy

Diagnosis:

- definite Ø = skin manifs + 3 other Criteria
- probable Ø = " " + 2 " "
- possible Ø = " " + 1 " "

Invs of DM

① · MS < Enzymes, Rad.: EMG, UIS, MRI (أحدث), Biopsy (EMG غير نوعي)

② · Skin: Biopsy → Non-specific.

③ Serology: Auto Abs. (Abs)

- Auto antibodies (أنواع)

[Serology is not sensitive so not useful in Ø.]

Highly specific

- 155 KDa (or Se) (80%) (Anti TIF1γ)
- Jo-1 (20%) (anti synthetase)
- Mi-2 (5%)
- SRP (5%)
- PL. 7 & 12
- OJ
- EJ
- KJ (Lung)

Antibodies of Anti-Mi-2 ss ew

Low specific

low titer ← ANA < speckled, Nucleolar
- Ss DNA
- Anti Ro
- PMSCL 70
- U1 RNP
- U2 RNP
- KU

Autoantibody	Significance / Association.
Anti-Mi2	• Classical DM (Most Specific), Responsive for ↑↑↑
• Antisynthetases or Aminoacyl tRNA Synthetases: • Anti-Jo-1 (thickest) • PL-7, 12 (Threonyl) • EJ, OJ	→ Antisynthetase Synd: – Raynaud's – Mechanics Hand – Synovitis – ILD = (interstitial lung dse) – Resistant to ↑↑↑ – Dx: Anti-aminoacyl tRNA synthetases.
• Anti 155kD/140 (TIF-1γ) (Transcriptional intermediary factor)	• Mg ass. & Amyopathic DM
• Anti-NXP2 (Annexin XI)	• Juvenile DM.
• Anti CADM 140	• CADM (clinically Amyopathic DM)
• Anti SRP (Signal Recogn.) particle	• Severe Polymyositis (Fulminant) ē resistance to ↑↑↑ & Cardiac & ILD
• pM-SCL • U2RNP • KU	} overlap ē Scleroderma. (Sclerodermatomyositis)
• Ro (SSA)	→ overlap è, SCLE, Neonatal LE

D Histopathology: (as SLE)

Treatment (علاج خارجي مع بعض)

- Myositis → Cs
- Dermatitis → as DLE
  - ↓ Calcinosis

Cut Manifs: (difficult to be Treated)

↓

as DLE (Sunscreens + Topical Cs + Antimalarials) or Tacrolimus & MTX

Myopathy → Cs

CPK اعلى

- mild cases (CPK < 1000 U/L)
  - ↓
  - Continous oral Cs (1mg/kg/d)
    - اسبوع على الاقل كله على ٤٠ واحد
- severe cases (> 1000 U/L)
  - ↓
  - Continous > 1mg/kg
  - Pulse or
  - Add other (Immunosuppressives)

NB resolve of Mypathy by Cs

Not always ass. ē improvect Cut. Manifs.

[↑↑ of skin dis; 2012]

THERAPEUTIC LADDER FOR DERMATOMYOSITIS

Systemic therapy (For Myopathy).

- Oral prednisone: 1 mg/kg tapered to 50% over 6 months and to zero over 2–3 years (1); option to use pulse, split-dose, or alternate-day (2) → mild cases
- Methotrexate: 15 mg/m² weekly (2) → severe cases
- Azathioprine: 2–3 mg/kg/day (3) → severe cases
- Others: → severe cases
  - High-dose IVIg (2 g/kg/month) (1)
  - Pulse cyclophosphamide (0.5–1.0 g/m² monthly) (2)
  - Chlorambucil (4 mg/day) (2)
  - Cyclosporine (3–5 mg/kg/day) (2)
  - Tacrolimus (0.12 mg/kg/day) (3)
  - Mycophenolate mofetil (1 g bid) (2)
  - Sirolimus (5 mg/day × 2 weeks, 2 mg/day × 2 weeks, then 1 mg/day) (3)
  - Infliximab (5–10 mg/kg q 2 weeks initially) (3)
  - Rituximab (375 mg/m²/infusion for 4 weekly infusions) (2)
  - Plasmapheresis (3)*

Cutaneous lesions (CLE, SCLE)

- Sunscreens (high solar protection factor including protection against UVA) (3) — Sun protect
- Topical corticosteroids (3) — Topical Cs
- Hydroxychloroquine (200 mg bid; increased frequency of drug eruptions in patients with dermatomyositis) (2) — Antimalarial
- Hydroxychloroquine (200 mg bid) plus quinacrine (100 mg/day) (3) — Antimalarial
- Low-dose weekly methotrexate (5–15 mg weekly) (2)
- Retinoids (3) — Retinoids
- Topical tacrolimus (3)

Others:
- Mycophenolate mofetil (3)
- Dapsone (3)
- Thalidomide (3)

Table 43.7 Therapeutic ladder for dermatomyositis. Key to evidence-based support: (1) prospective controlled trial; (2) retrospective study or large case series; (3) small case series or individual case reports. *Double-blind trial showed no benefit.

++ of Calcinosis Cutis:

(2C)
1. Cs
2. Probenicide
3. Diltiazem
4. Colchicine
5. Surgical Excision

Types of Calcinosis cutis in DM

1. superficial cut.
2. periarticular S.C
3. along facial planes in ms
4. skeleton affection

Skin
S.C.T
muscle
Bone

Table 43.5 — Calculation of the skin severity index (DSSI).

CALCULATION OF THE DERMATOMYOSITIS SKIN SEVERITY INDEX (DSSI)	
Site of cutaneous involvement	Degree of involvement score 0, no involvement 1, <10% involvement 2, 10 to <30% involvement 3, 30 to <50% involvement 4, 50 to <70% involvement 5, 70 to <90% involvement 6, 90 to 100% involvement
Head (A *h*)	0 to 6
Trunk (A *t*)	0 to 6
Upper ext (A *u*)	0 to 6
Lower ext (A *l*)	0 to 6

Symptom/physical finding	Severity of involvement score 4, very severe	3, severe	2, moderate	1, slight	0, none
	Head (h)	*Trunk (t)*	*Upper ext (u)*	*Lower ext (l)*	
Redness (R)	0 to 4	0 to 4	0 to 4	0 to 4	
Induration (I)	0 to 4	0 to 4	0 to 4	0 to 4	
Scaliness (S)	0 to 4	0 to 4	0 to 4	0 to 4	

DSSI = 0.1(Ah)(Rh + Ih + Sh) + 0.3(At)(Rt + It + St) +0.2(Au)(Ru + Iu + Su) + 0.4(Al)(Rl + Il + Sl) = Total score (0–72)

Ext, extremity.

DIFFERENTIAL DIAGNOSIS OF DERMATOMYOSITIS
1 **Systemic lupus erythematosus**
Physician might notice the nailfold telangiectasias and photodistributed poikiloderma but miss the muscle weakness, heliotrope, extensor distribution, and the violaceous hue (true lupus erythematosus might be present in the setting of an overlap syndrome)
2 **Psoriasis**
Involvement of elbows and knees with papulosquamous lesions can lead to misdiagnosis
3 **Airborne or allergic contact dermatitis**
Eyelid edema can be marked in dermatomyositis; look for additional sites of dermatitis
4 **Photodrug eruption**
Photodistribution
5 **Cutaneous T-cell lymphoma**
The poikiloderma often begins in intertriginous zones rather than on the scalp, face and extensor surfaces
6 **Atopic dermatitis**
Usually in children, where the physician focuses on the pruritus and secondary eczematous changes
7 **Scleroderma**
The nailfold telangiectasias are similar in appearance, but the dyspigmentation is quite different; edema of the hands is an early sign (true scleroderma may be present in the setting of an overlap syndrome)
8 **Trichinosis**
Patients have painful muscles and periorbital edema, but not other features
9 **Photodistributed form of multicentric reticulohistiocytosis**
Firm papules have distinct histologic features

Systemic Sclerosis

(Scleroderma)

Def: Autoimmune CT disease of unknow Etiology ch. By:

التعريف

△
1. Raynaud's Phenomenon.
2. Cutaneous sclerosis (Hardening)
3. Systemic (internal) organs sclerosis

NB: The dis. has 3 Names:

- **SSc** — مش دقيق لأنه مش لازم يجيلك فيه: Systemic = internal organ affect
- **Progressive SSc** — مش دقيق لانه "Not progressive"
- **Scleroderma** — الأصح

Scleroderma:
- Cutaneous (localized, circumscribed)
  - Morphea (Patchy, asymm, No Systemic affect) or Raynaud's
- Systemic (Bilat, Symm ± Systemic affect) → SSc

- Pathogenesis (see Morphea): Vasculopathy, Autoimm., Sclerosis
- Epidemiology:
  - Age: 30-40 Ys (85% appear in 20-60 Ys)
  - Sex: M:F — Generally: 1:3-6
    - L SSc: 1:10
    - d SSc: 1:1
- Clinical presentation:
  1. Clinical picture →
  2. Clinical Types
  3. Criteria for Dx
  4. Dx.

C/P of SSc

Triad of: Raynaud's, Cut. sclerosis, Systemic "

1. Raynaud's phenomenon:

- def. Episodic Vasospasm of digital arteries → Color changes (ē expose to cold.)

W → B → R

(white (VC) → Blue (post cap ven open) → Red) open of VS

في حالات: lSSc: بتحصل قبل الـ sclerosis أو معاها في نفس الوقت (بسنة)

" " " " : dSSc (بسنوات عديدة)

2. Cut. Sclerosis:

Has 3 phases (3 مراحل)

A. Edematous phase: (Stiff, puff Fingers)

B. Indurative " : (Sclerotic) (Taut shiny, Hide bound; waxy skin) (جلد مشدود - لامع - جلد سميك - شمعي)

C. Atrophic: (softened, burnt out).

Sclerotic skin appear:
- Smooth
- Firm
- Tight
- Shiny
- Yellow
- Hide bound

Site (مكان):
- lSSc: Acral (Face (90%), Hands ", Feet (10%))
- dSSc: Truncal (chest & proximal limbs) (+) Acral

- Other cut Manifestations: Dyspigm. - Calcinosis Cutis - Telangiect. - Pruritus, Palmar Erythema, Ulcers.

a. Dyspigmentation (Sdt.)

Hyperpigm. (more Common)

Diffuse Hyperpigm. (tanning) (دوزي)

Intensified over pressure areas as belt line & under brassiers.

(Addison Like Hyperpigm).

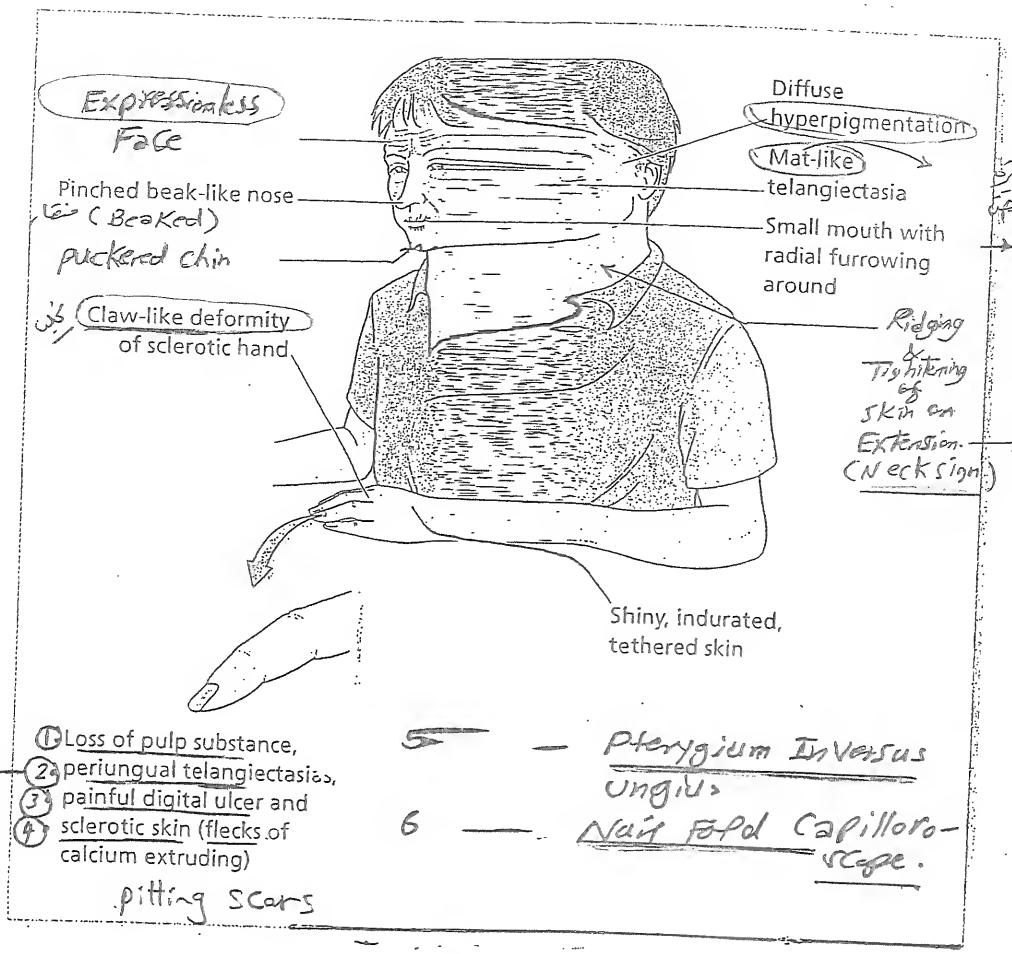
Hypopigm. (Leukoderma)

may affect NL (or) Sclerotic skin of Face & trunk →

- Leukoderma Except:

(VKA (Reticulum Vitiligo)) → b. Peri Follicular areas: (طبيعي) (Very chic sign = Salt & Pepper sign)

b. ± skin over Superficial veins



periaral Furrows

Groove.

علامة AUCTDs

1. Loss of pulp substance,
2. periungual telangiectasias,
3. painful digital ulcer and
4. sclerotic skin (flecks of calcium extruding)

pitting scars

5 — Pterygium Inversus Unguis

6 — Nail Fold Capillaroscopy.

NB

- Calcinosis Cu in SSc ch
- Called: Thiel Weissenbach
- ± Ass. ē Rese B bones of F nal phalanges

(D) Calcinosis Cutis: ..... as (DM)

- Usually at distal ——— joints.

(Dermatomyositis ؛ت تومض.)

(J) Telangiectasia (75%) — Face, lips, Hands [discrete, Mats like]

- also: there may be:

(A) Ulcers:

d.t ischemia → at tips of digits
Fibrosis
Trauma → Interphalangial

difficult ##### may → movement limitat, osteo
Autoamputat & depressi

(B) Xerosis & pruritus

(C) palmar Erythema, P ⟸ Papular lesions d.t ← Lymph. obstruction, Amyloid deposition, Fibrotic changes

(D) MM. affect

3 Systemic (internal) organs Sclerosis

4 systems mainly involved by SSc:

1. Lung
2. Heart
3. Kidney
4. GIT

Lung → die → 2 Forms of the dis

onset: dSSc → ≤ 5 yrs (diffuse skin involvement, early onset) / lSSc → > 5 yrs (limited skin involvement, late onset)

Interstitial Lung dis (ILD, 20%)

- Alveolitis → Pulm. Fibrosis
- Diagnosis:
  1. Pulm. Function tests (PFTs).
  2. CT (High resolution).
  3. Bronchoalveolar lavage

Pulm. HTN (PA)

- Diagnosis:
  1. Echo.
  2. Rt sided Heart Catheterization

2 Heart

- Palpitation.
- Friction Rubs.
- CHF

3 Kidney

- HTN
- Renal Crisis.
  - Accelerated HTN
  - → RF
  - Hemolytic anemia (Microangiopathic)

4 GIT

- Reflux & dysphagia.
- Constipation
- diarrhea.
- Impaired peristalisis
- Int. Obst.
- malabsorption

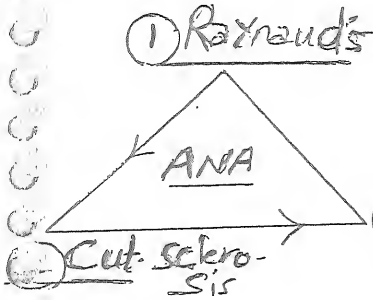
• Renal Crisis:

if SBP ↑ by (≥ 20) / DBP ↑ by (≥ 10) → From the baseline BP → Renal Crisis.

1. Clinical Types:

1. LSSc → LSSc (Acrosclerosis) / CREST Synd. (أو الـ TSSc)
2. dSSc
3. Transitory Form (LSSc / dSSc)
4. PreSSc — full extent of sclerosis (Not) reached
5. Overlap SSc (DM or SLE)
6. SSc Sine Scleroderma = (No) Cut. affect (only) Systemic

ما تنساش المثلث ده



	LSSc (Acrosclerosis)	dSSc.
Sex (M:F)	1:10	1:1
Raynaud's Phenom.	مع بعضهم occurs at same time or precede the cut. sclerosis by ≃ 1Y.	قبل بكتير occurs many Ys before Cut. Sclerosis.
Cut. Sclerosis	Acral	Truncal & ± Acral
Systemic affect	وقت طويل delayed affect (>5Ys from onset of Cut. sclerosis) • More PAH - dilatat without Significant drop out.	Early affect (في ≃ 5Ys from onset of Cut sclerosis). • More ILD • Dilatation & drop out (destruct) ← غير Micro Hge
Nail fold Capillaroscope (Elongated loops)		
Autoanti-bodies	(بالدم) - AntiCentromere (80) إيجابي - Anti Th/To - Anti U11/U12 RNP	(SCL70) ؟ - Anti-Topoisomerase I DNA "Bad prog (ILD)" - Anti-RNA Polymerase III (severe Cut + renal good prog) - also Anti fibrillin (U3 RNP) (Myopathy, Cardio, PAH)
Course (10 Ys)	• Slowly progressive • better prognosis • Survival Rate (70%)	• Rapid Progression • Bad Prognosis • Survival Rate: (20%)

NB The Following ē LSSc > dSSc = [Pulm. HTN, Sicca Synd.

- Anti Centromere < LSSc 80% / dSSc 30%
- Anti Scl70 (Topoisomerase) < LSSc 15 / dSSc 60

ACR Criteria For SSc

A. Major Criteria : (1)

(1) أو

- Symmetric Cut. sclerosis proximal to MCP or MTP joints.

B. Minor Criteria : (3)

(2)

(i). Sclerodactyly (sclerosis of Fingers).

(ii). digital pitting scars (or) loss of substance from Finger Pad

(iii). Bibasilar pulm. Fibrosis.

- For Diagnosis : 1 Major [or] 2 minor.

NB (نقوى) ← What is the leading Cause of death in SSc ??

نزل (حالياً)
- Was: Renal Crisis (But incid. ↓ ē use of ACEI)
- Now: pulmonary affect ✓

SSc Autoantibodies (10) → ANA (98%) [أكيد]

(هدل لوفيا اسبتال 316)

LSSc
- AntiCentromere (↑PAH)
- Anti Th/To (same PAH & ILD)
- Anti U11/U12 RNP (Severe ILD)

dSSc
- Anti-TopoIIsomeraseI (Bad Prog, ILD)
- Anti RNA Polymerase III (Better Prog) (Cut. Renal)
- Anti U3 RNP (Fibrillin)

Overlap
- Anti PM/
- Anti-K (Both Myositis)
- Anti UR

MCTD

CREST Synd. = LSSc

1. Calcinosis :. Calcofic deposits at ← Extremities around joints ~ Bony prominences.
2. Raynaud's — Commonest : Flexors of Hands & extensors of elbow & Knee (تكلس)
3. Eosophageal dysmotility = lower Part → ↓ Peristalsis
   - ↓ low Eosoph. sph. Pressure
   - Incomplete Relaxation of LES = lower Eosph sphincter
4. sclerodactyly
5. Telangiectasia

Site: dermal or (deeper)

Start at distal Fingers & progress proximally & may involve the Face.

- Rectangular or Elongated Shape.
- Vs appear close to each other → discrete mets like. (Not as in osler Rendu–

Andrews 171

- Other Clinical Features : as in (LSSc.)
- Autoantibodies : - ANA (Nucleolar).
  - Anti Centromere (30%)
  - others
- Pathology : as lSSc
- ~~HH~~ : ~ ~

DD of Morphea or SSC

"Morpheaform or Sclerodermoid Conditions"

(592)

DIFFERENTIAL DIAGNOSIS OF SCLERODERMOID CONDITIONS

	Clinical features
Mucinoses	
Scleredema	Induration of the upper back, neck and face; occasional internal involvement (see Ch. 46)
Scleromyxedema	Waxy papules (often in a linear array); diffuse induration favoring the face, upper trunk, arms and thighs; monoclonal gammopathy; neurologic, gastrointestinal and pulmonary involvement (see Ch. 46)
Immunologic	
Chronic GVHD*	Morpheaform plaques favoring the trunk, which may become generalized; eosinophilic fasciitis (see Ch. 12)
Eosinophilic fasciitis	Symmetric induration with a 'pseudo-cellulite' appearance on the extremities (sparing hands and feet) (see text)
Generalized morphea*	Expansion and coalescence of morphea plaques to involve a large portion of the trunk and extremities (see Ch. 96)
Fibroblastic rheumatism	Sclerodactyly; fibrotic nodules on the hands
Paraneoplastic	
POEMS syndrome	Sclerotic skin on the extremities (see Ch. 114)
Amyloidosis (primary systemic)†	Diffuse induration favoring the face, distal extremities and trunk (see Ch. 47)
Carcinoid syndrome	Sclerotic skin on the legs (see Table 52.3)
Neoplastic	
Carcinoma *en cuirasse**	Sclerodermoid encasement of the chest by metastatic carcinoma (usually breast cancer)
Metabolic	
Diabetic cheiroarthropathy	Thickened skin and limited mobility of the hands (see Table 52.4)
Porphyria cutanea tarda*,‡	Morpheaform plaques in sun-exposed areas (see Chs 49 & 96)
Neurologic	
Reflex sympathetic dystrophy*	Painful, cold, swollen extremity eventually develops cutaneous sclerosis (see Ch. 7)
Spinal cord injury	Sclerotic skin in affected areas
Toxin-mediated	
Nephrogenic systemic fibrosis*	Associated with exposure to gadolinium-based contrast agents (US, 1997-present; now worldwide) (see text)
Eosinophilia-myalgia syndrome	Associated with L-tryptophan ingestion (US, 1989) (see text)
Toxic oil syndrome*	Associated with toxic oil ingestion (Spain, 1981) (see text)
Drug- or chemical-induced (see text)	
Bleomycin*	Acrosclerosis, Raynaud's phenomenon; pulmonary fibrosis (more common, usually no concurrent skin lesions)
Taxanes	Edema followed by sclerosis of the lower extremities; acrosclerosis
Vinyl chloride, chlorinated hydrocarbons*	Acrosclerosis, acral fibrotic papulonodules, Raynaud's phenomenon, acro-osteolysis; pulmonary fibrosis
Venous insufficiency	
Lipodermatosclerosis*	Woody induration and hemosiderin pigmentation on the lower legs; may also involve the pannus (see Ch. 100)
Genetic disorders	
Restrictive dermopathy§	Tight, thin skin over the entire body; joint contractures; *LMNA* or *ZMPSTE24* mutations
Hutchinson-Gilford progeria	Sclerotic skin on the lower trunk, buttocks and thighs; *LMNA* mutations (see Ch. 62)
Werner syndrome	Tight, sclerotic skin on the distal extremities; *RECQL2* mutations (see Ch. 62)
Stiff skin syndrome*	Fibrosis of the skin/fascia of the buttocks and thighs with hip contractures (see text)
Phenylketonuria	Sclerotic skin on the thighs and buttocks with hip contractures (see Ch. 62)
Winchester syndrome*	Diffuse, symmetric, leathery skin thickening; fibrotic plaques or bands; *MMP2* mutations (see Table 69.2)
Ataxia telangiectasia	Tight, sclerotic facial skin (see Ch. 59)
Kuriez syndrome	Sclerodactyly; atrophic skin on dorsal surfaces of hands and feet; palmoplantar keratoderma (see Ch. 57)

*In overlap with morpheaform disorders, which are listed in Table 96.1.
†Primary cutaneous amyloidosis can also occur in patients with systemic sclerosis and generalized morphea.
‡May also be observed in patients with congenital erythropoietic porphyria and hepatoerythropoietic porphyria.
§Sclerodermoid changes are typically present at birth.

H-Synd

Table 44.6 Differential diagnosis of sclerodermoid conditions.

(3) - Scleroderma
- Scleromyxedema
- Scleroma Neonat

(4) - Shulman synd
- Stiff skin ns
- Nephrogenic systemic fibrosis

L.T.M → - Toxic oil synd
- Eosinophilic Myalgia Synd

- PCT
- GVHD
- PKU
- Lipodermato-sclerosis

- Amyloidosis
- POEMS
- Carcinoid Synd
- Carcinoma en Cuirasse

- Werne- & H Gil
- Ataxia Telang

- DM Cheiro athropathy
- Rh fibroblastic

- Synds (5)
- Drugs
  - Vit K
  - Vit B
  - Bleomycin
  - Taxanes
  - Hydrocarb

Scleroderma Related disorders.

1. Eosinophilic fasciitis
2. Stiff skin synd.
3. Nephrogenic systemic fibrosis
4. Eosinophilic Myalgia Synd.

1. Eosinophilic Fasciitis (Shulman's Synd.): See Morphea.

2. Stiff Skin Synd.

- Age: Cong. or Early childhood. (fibrillin gene Mutat=)
- Clp: Rock hard induration & thickening of skin & S.C.T mainly affecting buttocks & thighs with chic sparing of inguinal Area (Folds). X

Spar LY

X - Hands & Feet are spared.

- Ass: (a) Hypertrichosis
  (b) chic posture of Hip & Knee flexion (Joint restrict=) ∴ prominent lumbar lordosis while standing
- Course: → stable or slowly progressive. (without)
  XX Int. organ affection.
- Path: Thickened, Hyalinized (fascia) without an ass. inflamm. infiltrate X
  Dermis: ± Mucin & Collagen Hyalinizat=

Hh → No effective Hh
↘ physiotherapy → ↓ Joint Contracture.

Eosinophilic fasciitis = Shulman syndrome

Def: Acute onset of fasciitis → Followed By → Induration Similar to that of Morphea (+) Eosinophilia. (sclerodermoid picture)

- Epidemiology:
  - Age: 30-60 ys.
  - Sex: M=F.

- Aet. unknown but ± d.t: Inf. (Borr.) – drugs (Atorv.) – Autoimmune (ANA) – ort.
  1. Autoimmune → d.t ass. ANA & Hypergammag. ↑ γ globulin
  2. Environmental → drugs (Atorvastatin), Toxins & Radiation (↳ alter seven physical activity)
  3. Infection: Borrelia Burgdorferi
  4. others: ↑ TGFβ, ↑ IL5, ↑ CD8, ↑ Mangenese SOD & Tissue inhibitor of Metalo proteinas [TMP-1] (Marker of dis.)

- C/P: 3ơ. following strenuous physical activity

* clinically 3 stages:

1. 1st → Bilat. Symm. diff. Erythema & Tenderness.
2. 2nd (oedematous ph.): "dimpled appearance"
   - Coarse (Cobblestoning)
   - or Fine (Peau d'orange)
3. 3rd: rippling, Induration, Fibrosis, Hypopigm. (Woody skin)

(Erythema → edema → Woody skin)

→ "Pseudo-cellulite"

NB: Ass. ① Joint Contracture & Fibrosis
② Arthritis
③ Myositis
④ Neuropathy
⑤ Carpal Tunnel.

البعض يعتبرها نوع من الـ Morphea & لوبوس: خطأ

- pathology: Fascial fibrosis (fascia thickened (10-50) times NL), Dermal Fibrosis & fascial & subfascial ms Infilt.

- Diagnosis: - Fascial Biopsy & MRI
  - ↑ ESR & Eosinophils.

Treatment
① Cs
② others NSAIDs, MTX, PUVA

NEPHROGENIC SYSTEMIC FIBROSIS (NEPHROGENIC FIBROSING DERMOPATHY)

- def.: Sclerodermoid condition usually affecting RF patient
- Epidemiology:
  - Age: any but common in middle aged.
  - sex: M = F.
  - Risky patients:
    1- Renal impairment: sp. CRF with dialysis (90%)
    2- Chr. LCF.
    3- HyperCoagulable states.
    4- Surgical procedure
    5- IV dye (gadolinium)
- Pathogenesis: → Aberrant targeting of Circulating Fibrocytes to peripheral tissues (BM derived WBC).
- CIP → Bilat., Symm., Erythematous - Hyperpigmented plaques on Extremities & Trunk with irregular advancing edge (Amebotid appearance)..
  - Ass: ① Joint contracture
    ② Yellow sclerae plaques
    ③ systemic fibrosis of Heart, Lung, ms.
- Pathology: - Haphazardly arranged Collagen bandles
  - ↑Mucin deposit
  - ↑ fibroblast cells that stains +ve for CD34 & ProCollagen I
  - (±) Gadolinium particles (by spectroscopy)

Refractory ← ## → 1- Renal Transplant
2- Immunosupp.
3- PDT 4- pharesis 5- IVIG 6- UVA1 كريمة

Antimalarials (Mad)

- **Mech.**
  1. Immunomodulating → ↓ IL2 product
     ↓ MHC expression by Macrophages.
  2. Anti-inflammatory
  3. Antiplatelet (so used in APS).
  4. Photo protect (in PCT) ← In PCT Chelate Porphyrin
     - Chloroquine → 250 mg (Dagrinol ®), Alaxoquine ®
     - Hydroxy Chloroquine → 200mg Plaquenil ® & Hydroquine
     - Quinacrine → Atabrine 100 mg ®

- **Kinetics:** - Metabolized by liver
  - (50%) Excreted via Kidney
  - Half-life 50 ds (slowly released → delayed onset of effect ē in (3-4 ms) (or 6-8 ws)

- **Indications:** 1. LE (Ctl- AICTD) الأكثر
  2. PMLE
  3. others: L.P, GVHD, (PCT), GA, Sarcoidosis, DM & (APS).
     Choroid يتركز في ← ...ē

- **S.E:**

1- Common: "Pigmentary"

↓ (i) Hypopigm. of Hair

↑↑ (ii) Q & HQ → Blue-Black pigm of: skin, MM (Hard palate) Nail, sclera & Cartilage.

(iii) Atebrine: Yellow pigm. of skin & Conjunctiva

2- un Common

(i) - NV ← Nausea Vomiting

(ii) Hepatotoxicity

(iii) Irritability

"ē Non-dermatological Antimalarial" → anemia in G6Ph deficient Pts.

3- Rare

(i) Retinopathy:

* Visual field defe... to (red) objects & Paracentral Scotom...
* Q > HQ. Atebr... has No Ocular S...
* Early reversible later Non revers...

(ii) CBC: Hemoly...

(iii) others:
- PS. (↑↑)
- Rash & FDE
- EM

NB: to ↓↓ ocular S.E:

1- Sunglasses
2- Eye Exam / 6ms
3- Stop after 6ms (or) at winter
4- ↓ dose after improvement (±) Atebrine

- C.I: ① Hypersensitivity
② Impaired liver
③. BM --
④. Retinopathy

- preg. & Lactat: Category C

(American Acad. of Ped.)

- Interact: 1- Cimetidin → ↑ level

أدوية بتأثر على الكبد → 2- Kaolin & Mg Trisilicate: ↓ Abs

3- Q & HQ should be avoided but Atebrine may be combined

لازم يبطل 4- Smoking. بيقلل مفعول الدوا كتير

- Dosage (½ - 1 حبة)

1- Q → 125-250 mg 1d (or 3.5-4 mg/kg/d)

2- HQ → 200-400 mg/d (or 6.5 mg/kg/d)
(1-2 حبة)

3- Atebrine: 100 mg 1d.

4- In PCT ??. Q: 125 mg twice/w مرتين
(الدم) HQ: 100 mg Trice/w ٣ مرات

Treatment of SSc

1. ## of Raynaud's (See below)

2. ## of Sclerosis: (usually (non) effective) → Antifibrotics:

- D-penicillamine.
- Colchicine.
- Griseofulvin
- Trental
- MTX
- IFN (α & γ)
- cyclosph.
- Phototherapy. → (UVA1)
- photopheresis.
- Tyrosine Kinase Inhibitors: (Imatinib.) (TKI)

3. ## of ulcers:-

- ## of Raynaud's
- Minimal Mechanical debridement
- Moist occlusive dressing (Hydrocolloid)
- Topicals: Collagenase, PDGF

4. ## of Calcinosis Cutis:

(3C)
- Cs
- Colchicine
- CCB

- Warfarin
- probencid
- Deltiazem

- Alum - hydroxide
- surgical

5. ## of Complicat:

(PAH) - Pulm. HTN → O2 & Anticoagulant; Epoprostenol (PG) & Sildenafil & Bosenton (Endothelin Rs)

(ILD) - pulm. Fibrosis → Cyclophosphamide. ± (Cs + MM)

- Renal Crisis → ACEI
- Reflux osoph. → Proton pump inhibitors. PPI; promotility Agents (ondansetron)

Mixed Connective Tissue dis. (MCTD)

Em Bsp. (2004)

(MCTD = Mixture of B)

doesn't fulfill criteria of one of them

def disorder in which Features of many CTDs

as SLE, SSc, DM, SS

Can Co-exist & overlap

- Considered as a distinct Synd. ē specific Serology & Shouldn't be confused ē "overlap Synd" in which there is Combination of diseases where each complies ē diagn. Criteria for That disorder

- Ch By: 1- Course → - chr. & milder than other CTDs.

Considered as intermediate stage مرحلة وسطية

& eventually becomes either

SLE or SSc

2- Specific Marker → Anti U1-RNP

- AEt: unknown but ± ass ē:

1- HLA DR4 (or)

2- Genetic predisposition.

- ↓: ANA (speckled), Anti U1RNP
- ↑: ESR

- Age: 30-50 yrs (in children Course ± severe ē ↑ incid of: Heart, Kidney, Thrombotic cytop.)

- Sex: M:F = 1:4.

- CIP

- Raynaud's phenomenon → Most Common presentation & First to appear.
- Arthralgia/Arthritis
- Esophageal Hypomotility
- Pulm. dys f. (Pulm. HTN)
- Renal → SI.
- Swollen Hands
- Myositis
- Rash
- Leukopenia
- Vasculitis: SLE, Alopecia, Erythema → Heliotrope E, Gottron's

Never Sclerodactyly

Raynaud's

Sausage digits

U1-RNP

Dactylitis

Arthritis

Eosopha. Cut. pulm.

ESR

Sjogren's Synd (sicca = Mikulicz dis.)

def Autoimmune dis. That affects primarily secretory glands sp < lachimal / salivary & has classical △ of:

- KCs.
- Xerostomia.
- Arthritis

others
(i) cut.
(ii) systemic

NB. Has muco cut manifs that may be the first presenting signs.

@ may be The 1ry or Ass. ē < R.A (+++) / SLE, scLE / SSc / MCTDs

3 Types
- 1ry
- 2ry
- Juvenile

CIP: European Community Criteria For Dg of SS:

eye & tongue:
- Xerophthalmia.
- Xerostomia.
- Corneal damage

Salivary:
- Impaired salivary gland funct-.
- Salivary gland Lymphocytic infilt.
- +ve Autoantibodies (Anti Ro (SSA) & Anti La (SSB))

Sge: any but common in 30-50

Sex: M:F 1:9

التشخيص بالمختبر ✓ (+) Anti alpha fodrin Ab

① - Xerophthalmia:-

- (KCS) or dry eye Synd ch BY chronic dryness of Cornea & conjunctiva.
- Discomfort (redness, burning, itching & FB sensat-).

② Xerostomia:

- Dryness.
- Tongue: → Red, smooth & dry
- Dental Caries
- oral Candidiasis
- perteche

3 glands ← Parotid & sumb mandibular & maxillary gland Enlargement.

③ - Other mm:

- Atrophic changes of:
  - URT → Nasal dryness & Inf. (Atrophic Rhinitis)
  - Vulva & Vagina → Vaginitis.
  - Anal & Rectal → pruritus & Inflamm.

④ - Cut. Manifs

- Dryness & Xerosis → Pruritus.
- Dryness of Hair → brittle, Fragile & generalized Alopecia.

- Dryness <
- Erythema <
- Vasculitis of L.L
- Alopecia

- Erythema of Nose & cheeks
- Vasculitis (Post Capillary Venules of L.L)
- Erythema Nodules plaques:
  - Sweet Synd. like annular Ery.
  - SCLE like
  - Papular Erythema

- ↓ consciousness
- Immunosup

Serology
- Anti Ro Fetdin (70%)
- Anti Ro ISSA (60%)
- Anti La ISSB (20%)

⑤ - Extraglandular manifs:

1. GIT
   - E. dys
   - HSM
   - Abn oesoph. motility
   - Splenomegaly
   - Pancreatic affect
   - Hepatitis
2. Lung
   - Pulm: Fibrosis, HTN, Inf.
3. UT
   - irritated UB
     - Frequency
     - Nephritis
     - RT Acidosis
4. CNS
5. Arthritis

Antiphospholipid Syndrome (2012) (2014)
(APS)

Def. Autoimmune disorder dx By Triad of: △

1. **Thrombosis:**
   - * (≥1) arterial, Venous or small Vs Thrombosis in any organ Confirmed by doppler or HP.
   - * Affected organs (±) Cerebral, Cardiac, pulm., Adrenal, ocular, Musculosk. or peripheral.

   لو عندي شخص
   - Age ♂<55 ♀<65
   - No risk factor
   - Attack of
     - stroke
     - MI
     - DVT
     - pEmbolism
     - Adrenal Hge.

2. **pregnancy Morbidity:**
   - Early abort < 10ws. (≥3) Consecutive, Spontaneous (unexplain)
   - Late abort > 10ws: (≥1) Spontaneous abort
   - preterm labour ≤ 34ws: because of ← Eclampsia, preClampsia, placental insuff

3. **Autoantibodies ≥1**
   - Anti-Cardiolipin / phospholipid (aCL): IgG > IgM (أقوى)
   - Lupus Anticoagulant ab (LA) → (يعاد مرتين متقطعتين (12 أسبوع))
   - Anti-β2 Glycoprotein I.

For Dx = 1 lab + 1 Clinical

other

- Manifestations

1. **Cut.** (4A)
   - Livedo Reticularis (8%) (A)
   - Atrophdie blanche
   - ACro Cyanosis
   - Anetoderm
   - Alopecia
   - Raynaud's
   - Leg ulcers
   - Thrombophlebitis
   - Vasculitis
   - Blue-Toe synd.
2. **Neuro** migraine, Seizures, Multi-infarct dementia.
3. **CVS**: Murmur, Valvular Vegetations.
4. **Blood** Hemolytic anemia & thrombocytopenia

- Lab. Invs
  - APTT
  - False +ve serology of ⊄
  - CBC

2 varieties of APS

① Seronegative APS (like) synd.: The same clinical Manifs but (-ve IMVs)

② Catastrophic APS: Severe, progressive with multiple Vs affect⁻; fatal within few days. (Tt: IVIG, Cs, Rituximab)

• Etiopathogenesis: There are 2 Types of APS:

- 1ry APS (Not ass.ē any underlying dis.)
- 2ry APS (± ass.ē systemic illness):
  - (i). AICDs: SLE, SSc, MCTDs & RA. (& ± BD)
  - (ii). Infect⁻: HCV, HIV, $, Malaria
  - (iii). Drugs: . Cardiac: BB, Hydralazine, Procainam
    . Neurological: phenytoin
    . @thers: "Amoxicillin" & IFN-α.

- on Both Types there are product⁻ of Many autoabs → Thrombosis → placental affect⁻ → pregnancy Morbidity:

- these antibodies Include:
  ① ACL abs (Antiphospholipid): against memb. phospholipids
  ② Aβ2 Glycoprotein I: plasma Protein associating memb. phospholipids
  ③ LA. Abs: (misnomer Not related to lupus Nor No Coagulat⁻ but theres Thrombosis): Abs against Coagulat⁻ factors (prothrombin, Protein C & S, Annexins, LDL → atherosclerosis & MI).
  ④ defective platelet & endothelium of BVs

pregnant ē
HX of loss
• Heparine + Aspirin (8wks) prenatal & post partum then Warfarin

• Tt of APS (No specific Tt)

1ry thrombo. prophylaxis:
- prophylactic (Tt ↓ risk of 1st ever)
  ① General step < Smoking, ocps
  Tt < HTN, Hyperlipidemia (statins)
  ② Aspirin (?? low dose) or Clopidogrel (if Allergic to Aspirin)
  ③ Hydroxy chloroquine: APS ass.ē SLE (Antithrombotic effect)

2ry thrombo prophylaxis
- Thrombosis: IV or S.C Heparin → Then Warfarin (adjust ↙ Venous INR = 2-3, Arterial = 3) (for life)
- Allergy to Warfarin: Newer Agents Antithrombin & Factor X Protein ass. Rituximab

Raynaud's phenomenon (EM, Bologna, D.N).

Def: Vaso spastic dis. ch^ By Episodic Reduction of Blood Supply to the Fingers & /or Toes mainly in Response to Cold Exposure.

C/P: ⊙ Affected fingers or Toes show at least 3 Color changes:

بنفس الترتيب (W B R)
- White (Pallor)
- Blue (Cyanosis) [↓Flow]
- Red (Hyperemia) [↑ Flow]

} usually reversible

⊙ There are may be < Pain / Numbness / digital ulcers. / other CTD manifestation

- **Types of Raynaud's ph.:**

① **1ry Raynaud's ph.:** (Raynaud's dis.) أو — Common, Younger girls — No any underlying Medical Problem.

② **2ry Raynaud's ph.:** uncommon & occurs in associat^ with other problem specially SSc

أسباب - **Conditions Ass. with Raynaud's Phenomenon** (2ry Rayn.)

1] AI-CTDs:
- Scleroderma (SSc)
- SLE
- MCTDs
- DM/PM
- RA
- SS

2] Inf.
- HBV
- HCV (sp. ass. ē mixed ⊕ Type III Cryoglob.)
- Mycoplasma (ē Cold Agglutinins)

3. Neoplastic:

- Leukemia
- lymphoma
- MM
- Carcinoma
- Polycythemia
- Type I Cryoglobulinemia

4. Environmental:

- Vibral injury
- Frostbite
- lead & Arsenic exposure
- Smoking.

esp → 5

5. Metabolic / Endocrinal:

- DM
- Acromegaly
- Myxoedema
- Pheochromocytoma
- Fabry's dis.

6. Hematological:

- PCRV.
- PCH.
- Cryofibrinogenemia
- Cryoglobulinemia.

7. Drug:

- CPs.
- BB.
- CyA.
- Bromocriptine
- Ergot Alkaloids

8. Syndromes:

- Carpel tunnel
- Thoracic outlet

← paraneoplastic Acral vascular synd.

- Asthetosclerosis
- Vasculitis
- Acrocyanosis

- livedo Retic.
- chilblains.

How to differentiate bet 2 Types of Raynauds.

	1ry Raynauds (Rayn. dis.)	2ry Raynaud's
• Incid	• More Common	• less Common.
• Sex: M: F	1 : 20	1 : 4.
• Age:	< 25 Ys	> 25 Ys;
• Ppt. of Attacks	Cold, Emotional stress	Cold
• No of " :	< 5 Id. (Bilat. & symm.)	> 5 Id (Asymm., ≥ 1 digits ± affected
Ischemic Injury	(good prognosis)	present (Bad. prog.)
Abnl Capillroscope		" pitting scars
• ANA	Absent.	+ve (> 90%)
• Anticentro-mere	(-ve)	+ve (30%)
• Anti SCL 70		+ve (70%)
• platelet activat^ (inuive)		+ve (90%)
		dilution drop out > dermo-scope

(HH)

① General Measures:

A – Avoid Smoking & Drugs as BB

B – Avoid Cold & Emotional Stress

C – Abortive of attack → Whirling arm (Soft ball Pitch) (Gesi) maneuver: arm Swinging 360° Circle → restore circ SSc.

② Specific HH

• 2ry Raynaud's → HH of underlying (AET)

• 1ry N

↘ • CCB → ↓ BP (ا ب ا) epilate 20-60 mg

↘ • ACEI **

• PGs

• Sildenafil

Cut. Manifs of Rheumatoid Arthritis (RA)

(جلدی اور کڈی)

Non-specific (General)

- Skin: pale, Atrophic, Fragile → Easy bruising, palmar Erythema
- Nails: Brittle

Specific

1. Palisading granulomas → Rh. Nodules, GD
2. Neutrophilic dermatoses
3. Vascular
4. Cut. manifs of → Felty's, Stills di
5. Drug Related.

---

(1) Rh. Nodules

- Most Common Cut. Manifs.
- Ass. ē High or Mod. titer ↑ RF & usually at late stage of dis (لکیر ہمیشہ بیری Arthritis جلد آخر)

→ Asympt., firm, semimobile Nodules at extensor surfaces
- of joints e.g Fingers, Heel, forearm, back, scapula, sacrum (کہنی)
- Can affect Visceral organs (lung, Heart, ms)

- if it appears in large No after MTX ↓↓ → (MTX induced Accelerated R. Nodulosis) (عدد)

Path:
- Central Zone: Eos, Fibrin & Cell. Hyalinized
- Mid Zone: palisaded Histiocytes.
- peripheral Zone: Vascular CT & mixed infilt.

NB Rh. Nodules like lesions + -Ve RF → S.C GA (عیر لیبر RF in ↑ titer)
or Any other palisading granuloma.

↓↓ Surgical Excision, ILs (یہ نہیں)

(Pseudo Rh. Nodules)

Differences from the subcutaneous nodules of rheumatic fever include more fibrinoid maternal, little cellular infiltrate and minimal zoning and fibrosis in rheumatic nodules. Nodules from patients with still's disease resemble histologically those of rheumatic fever.

GD (Granulomatous Dermatitis)

Interstitial GD (IGD)	Palisaded Neut. GD (PNGD)	Drug induced GD
C/P. Annular or linear (Rope sign) Erythematous plaques at lat. – Trunk, Thighs, buttocks & Axilla – occur in Both (RA or Sero-ve Arthritis)	Psoriasiform lesion. Crusted, umbilicated Papulonodules at Elbow or dorsal Hands. Ass: Rh, SLE, ANCA+ve Vasculits (Churg Straus)	ACEI, CCB & BB, Statins. C/P erythem. Vidu Pap., Nod & Plaques Flexures & thighs (Rapid Eru)
HP. Rosettes of Palisading Histocytes surrounding foci of Degenerated collagen	Neutrophilic infilt. & foci of LCV or as IGD	ILCs, Dapsone. HP: Interstitial Histiocytes Variable degen. elastic fib.
DD: Patch GA, leprosy, morphea	Rh. Nodules, Papular GA	

(2) Rheumatoid Vascular lesions (4):
- Vasculits
- Capillaritis
- Barwaters Histocytes

(1) Vasculitis ← Cut. (Urticarial) / ocular / systemic

(ii) Baywaters Nodules:
- C/P, Small, painful, purpuric Nodules at pulps of digits
- Path: SVV & (Ve) systemic affect.

(iii) Capillaritis: (pigmented purpuric Dermatosis)

(iv) Intra Vascular / Intra lymphatic Histiocytosis:
(Erythema, Indurat, papules over swollen joint sp. Elbow)

(3) Neutrophilic dermatoses: [PG, Sweet]
- Rh. Neutrophilic: Dermatitis, Panniculitis

(i) PG
(ii) Sweet's synd.
(iii) Rheum. Neutrophilic dermatitis: (Neutr. Vascular react.)
- Bilat. asympt. persistant Erythm. Nodules & plaques that may ulcerate at Extensor Forearm & Hands. (urticarial like)
- Hist. & Clinically: as sweets (diffuse dermal Neut. infilt. & Papillary Microabscess)

DD ← sweet ~ urticarial like → DD

DD of Sweet:
(i) No ~ Tenderness / Systemic manifs
(ii) Site.

(vii) Rheum. Neutrophilic Panniculitis: Panniculitis Nodules of L.L → ulcerat & drainage.

④ Cut. Manifs of:

(i) Felty's Synd: Severe subtype of RA

Ch BY Δ of:
1 - RA.
2 - Neutropenia
3 - Splenomegaly +
- Leg ulcers (PG like)

(ii) Still's dis: Juvenile Idiopathic (Rheum) Arthritis.

2 Types: Systemic onset (SOJIA) (<16y, M
Adult onset (AOJIA) (20-40, F

· CIP

Systemic
- Spiking fever
- Rash
- Sore throat
- Arthralgia
- L-N
- HSM

Cut.
(i). Asympt, Evanescent, ± (linear) macules, papules & plaques at pressure or Trauma sites.
(less common)
(ii) periorbital Edema
(iii) Linear, persistent, pruritic, Violaceous papules & Nodules (Lp like)

Lab
- leukocytosis
- Anemia
- ↑ ESR / CRP
- ↑ Ferritin.
- +ve ANA
- -ve RF.

⑤ Complications of Therapy.

(i). NSAIDs → pseudoporphyria & TEN

(ii) MTX → MTx Induced Accelerated Rheum. Nodulosis (at Hands)

(iii) TNF Inhibitors
- React at site of infect
- urticaria & Vasculitis
- GD
- PP Pustulosis

What's ??
- Rheum. Nodules
- // Nodulosis
- Rh. papules ?? (PNGD)

Sclerodema = Sclerosis

Def. Chr., Idiopathic, Inflammatory disorder that may affect the skin &/or systemic organs & ch BY "sclerosis" (Excessive Collag deposit + ↓ No of Fibroblast)

- It includes: (Sclerosing skin disorders)
  1. Morphea
  2. SSc → See CTDs
  3. LS → See lichenoid dermatoses.
  4. Morphea-form / sclerodermoid disorders.

⊙ NB: Fibrosis: ↑↑ No of N Fibroblast

Morphea & SSc..

Localized / Cut Scleroderma (Morphea)

* ch BY:
  - patchy, Asymm. (- ليتاري)
  - No sclerodactyly
  - No Raynaud's
  - No Systemic affect
  - NL Nail fold capillaroscopy.

* Types:

1. Plaque (Circumscribed) Morphea
   - classical
     - Guttate
     - Nodular (Keloid)
     - Bullous
     - APP.
2. Generalized Morphea.
3. Linear Morphea: (face / limbs)
   - Linear M. of Limbs
   - en Cup de Sabre (face)
   - Parry-Romberg synd.
4. Deep Morphea (Pansclerotic M = Morphea profunda)
5. Mixed Type.

2 diffuse = Systemic (SSc = Sclerodema)

ch BY:
- diffuse, Symm.
- sclerodactyly
- Raynaud's
- systemic affect: ± (Int. organs)
- Abnl Nailfold Capillaroscopy.

2 Types:
- lSSc
- dSSc

- NB Morphea According to the Depth of Sclerosis:
  1. Superficial (Dermal): Circumscribed plaque & Generalized
  2. Deep
     - deep dermis, S.C.T, fascia, ms, Bones, Meninges & Brain → Linear Type
     - M-profunda: S.C.T & fascia

Pathogenesis of Scleroderm

Triggers → Triad ← Vasculopathy, Autoimmunity, Fibrosis or sclerosis

SSc

- Genetics: HLA B8 & DR3
- Cosmetics: silicone
- Solvents: Benzene
- Free Radicals.
- Drugs ← Vit K & B, DP ✓, Cocaine.

Morphea

- Genetics: in M. profunda.
- Trauma
- Vaccination
- Infection: Borrelia Burgdorferi
- Radiotherapy

↓

[1] Vascular Injury (Very early):

- Micro Vascular injury of endothel of Capillaries →
  - ② Endothelial changes ← Swelling, Thickened (reduplication), Hyperplasia
  - ⑥ ↑ Endothelial cell markers
    - E1
    - sVCAMs
    - sE-selectin
    - VEGF
  - this Injury → Hypoxia

[2] Auto Immunity

CD4 → differentiation → Th2 → IL4, TGFβ → ++ Fibroblast → Excessive Collagen (Sclerosis)

[4] Others

Borrelia Burgdorferi → Penicillin

[3] Excessive Collagen deposit (I, III, V, VII) also other EC matrix

- Fibronectin
- proteoglycans

Triggers → Vascular injury → Hypoxia → Auto immunity → Excessive Collagen deposit

Morphea (See pathogenesis & classification)

(Localized or cut. scleroderma)

- **Epidemiology**
  - M > F
  - Age (usually < 18 yrs)
- **Types:**

① Plaque Type:

- **Size of Lesion:** 2 - 15 cm
- **Site:** asymm. on Trunk
- ____ : 3 stages

[1] Oedematous stage:

- Edematous, Indurated, Erythematous or Violaceous plaques.

[2] Sclerotic stage: lesions show:

- ⊙ **Center:** Sclerotic (Hard), Smooth, Ivory Waxy, White (with) loss of Follicles & Sweat glands.
  - Smooth
  - Ivory white
  - Waxy
  - Sclerotic
  - XX - lost ≠ Follicle, Sweat glands
  - ± PIH
  - [post inflam hyperpig]
- ⊙ **Edge:** Active, advancing shows Erythem-Violaceous Color & Telangiectasia

Improve ē ttt active ← داكن = (Lilac-ring) أو (غير واضح)

[3] Atrophic Stage: (after ms — ys): skin Softening ē Dermal Atrophy (50%)

NB: Postinflamm. Hyperpigm.: may demonates over sclerotic lesions & involute after sometime.

↓ Non active — Not improve ē ttt

Variants of Plaque Morphea:

① Guttate ; Multiple, small, chalk-white lesions without Induration (d.t superficial pathology)

- Both diseases Called : "White spot diseases"
1. Guttate Morphea
2. LSA
3. IGH
4. Guttate Vitiligo
5. Arsenic
6. Guttate Ps

- D.D : LSA but there are (No)
  - ← Epid. Atrophy
  - ← Follicular plugging.

② Nodular (Keloid) : Keloid like nodules or streaks in presence of Typical plaque (like) Morphea. (usually: indistinguishable from Keloids)

③ Bullous : subepid. bullae on Top of Morphea lesions. (d.t stasis of lymphatic fluid).

④ APP : "Atrophoderma of Pasini & Pierini" (مجهول)

- May represent very superficial or abortive (bu...) Form of Morphea. "More in Females"
- Paches Chi By
  - Hyperpigmented, Mv lilac ring.
  - minimal induration
  - depressed border "cliff-drop" (sloping)
  - & Well defined (Chi)
  - usually on Trunk specially the Flexures & may follow the: Blaschko lines (Linear A. & Moulin)

- similar to Morphea in: clinical & hist. Similarity to regressing plaque of morphea (Atrophic Stage)

Path: epid. Hyperpigm. dermal Atrophy. Coll. Hyalinization & Clumping.

Sevère S.C loss.

- 2 Conditions ± occurs at same pt.

good prognosis

tt : - Not effective

- ⊕ Spont. Resolution ∃in (ms - ys)
- For Borrelia: oral Penicillin or Tetracycline (for 2-3 wk)

② Generalized Morphea:

- More Extensive & severe form of plaque Morphea (That) affect Large Area of skin

X But Without → sclerodactyly
→ Raynaud's
→ Systemic affect

نزل عن SSC

- C/P: Start at the Trunk & rarely Extend to Acral Areas (Hand, Feet & Face) ⇒

(±) • May be ass. e:

- Dyspnoea: d.t chest involvement
- MS Atrophy.
- Anti-Histone Abs.

③ · Linear Morphea: (Linear Scleroderma) differ from plaque Type in:

· Age → Childhood (1st 2 decades).

· Serology: → high ANAs. (Homogeneous)

· depth: → deep dermis, SCT, muscle, bone ± meninges. (Fixed to underlying structures; Not as Morphea).

Variants

ع الأطراف

Linear Morphea of Limbs (LL>UL)

may be ass. ē:

① Spina bifida occulta.

② Faulty Limb development (Atrophy) & Joint Contracture.

③ Calcinosis Cutis

④ Melorheostasis: Cortical bone thickening

⑤ Concentric Rings around the limbs → Pseudoainhum.

ضربة بالسيف ع نقم الجبهة

en Coup de Sabre (Frontoparietal Morphea)

- Paramedian or Median depression or groove at Frontoparietal area of scalp.

· May extend:

· deep → even to meninges & brain.

· to scalp → Cic. Alopecia.

ضمور الوجه

Parry-Romberg Synd. (progressive Hemifacial Atrophy)

· Etiopathog. ?? Autoimmune, subtype of Morphea or d.t sympathectomy

· Epid. F>M, 5-15 ys.

① CNS: Trigeminal Neuralgia, Migraine & seizures.

② ocular: Enophthalmos, Horner Synd.

③ oral: delayed Erupt of teeth, dental Root Exposure & Resorption, difficulty in opening the mouth.

① Hemifacial Atrophy: severe Segmental (along Trigeminal) Morphea. differs from other types in:

- Primarily start at deep dermis, SCT, ms & Bone
- No Sclerosis (WLS) (not L.S.)
- Hyperpigmentation. Facial Hemiatrophy → Asyme.

② Alopecia.

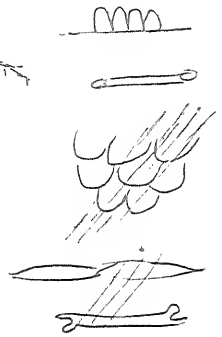
③ Epilepsy.

④ Enophthalmos.

4. Morphea profunda = disabiling Pansclerotic

- Morphea affect the S.C.T & underlying structures as the fascia. Most debilitating Type of Morphea.

- C/P: Indurated plaques ch BY:
  - ill defined (Cuz it is S.C).
  - have Cobblestone or pseudo Cellulitte appearance. (or peau d'orange)
  - shows groove sign: depression along the course of vein, between ms. groups or both.



- may affect the entire Trunk or Circumference of the limb. SCC May be a Complicat=

Pathology of Morphea (Δ as pathogen

1. Vs changes: Endothelial Swelling & Edema (Early stages at Lilac ring)
2. Autoimmunity or Infilt.: Retic. dermis & Trabeculae of S.
3. Collagen degen. = Homogenizat= = Thick Coll., closely packed, Hypocellular ē Mid-dermal "Trapping" of ECCrine gland (dermal-SC junct=)

	Morphea	LSA.
Epid.	NL (No) Follicular plugging	(Thining of Rete) NL Follicular plugging
DEJ	(No) Hydropic degen.	Hydropic degen. ē subepid. bullae.
Dermis	Homogenized Collagen (lower) ē mid-dermal ECCrine Trapping Elastic fibs → NL.	Edematous Coll (upper) Absent Elastic (Elastic)
S.CT	Inflamm. Fibrosis	(No) Inflamm. (mor) Fibrosis.

Morphea: Coll. Hyalinized & extend.

DD of Morphea 1- Morpheaform Condt=
2. SSc 3. Sclerodermoid Condit=

(SMAD can Exist 2d2)

Treatment قليلة — Penicillin

effective only during Active stage not Burnt-out Morphea

(لازم يبدأ من أول ما يظهر وتشخص الورم)

. Topicals

Penicillin

phototherapy — Cs + MTX or MM

(A) Limited plaque Morphea

No response after 2 ms.

1st line

. Topicals
- Cs
- ILCs
- Calcineurin --
- Daivobet (under occlusion)
- Aldara . (3-5 times/w)

Failed →

2nd line

localized phototherapy. (UVA1, PUVA > UVB)

لو مفيش نتيجة للعلاج الموضعي

(B) Generalized Morphea Eout

Joint. Contracture (3 lines)

phototherapy → (8 ws Failed) → monthly Pulse Cs + Weekly MTX → (Failed 2ms) → MM (Antirheumatic)

(C) linear of face or Joint Contracture

Pulse Cs + MTX → (Failed) Add photo th. → (Failed) MM

---

a Phototherapy : . UVA1
- Bath PUVA (3mg/L psoralen لوضع الجزء المصاب في الماء ثم ينتظر دقيقة ثم يتعرض ... إلخ)
- NBUVB
- RePUVA

30 J/cm² for 36 Session

then stop (الجسم بيتعود عليه) except linear

Interface dermatitis (Diseases affecting DEJ = lichenoid Dermatoses)

classification

Def.: inflammation of interface between epidermis and dermis (at DEJ), there are 2 types:

1- Vacuolar type :

Interface dermatitis is dermatitis in which there is a degenerative change at the dermal–epidermal junction, with inflammation (mostly lymphocytes) mostly at the interface between the epidermis and dermis. *Liquefaction degeneration, vacuolar alteration* and *hydropic degeneration* are three synonyms for this degenerative change that occurs at the basal layer. Tiny vacuolar spaces appear at the dermal–epidermal junction, often leaving the junction indistinct (Eosinophilic blobs) at the basal layer and superficial dermis are called colloid bodies (dyskeratotic cells, hyaline bodies, Civatte bodies). They appear to represent altered collagen or basement membrane, fibrin and immunoglobulin, as well as degenerated keratinocytes. Melanin incontinence also frequently occurs in any interface dermatitis. Interface dermatitis may be divided into the *lichenoid type* and the *vacuolar type*, the latter having a less impressive inflammatory infiltrate.

- DM
- EM & EDP
- GVHD
- LS
- AIDS/HIV

- Dermatomyositis DM
- Drug eruptions (sometimes)
- Erythema dyschromicum perstans EDP
- Erythema multiforme (sometimes) EM → prototype
- Graft-versus-host disease GVHD
- Interface dermatitis of HIV infection
- Lichen sclerosus LS
- Lupus erythematosus LE
- Secondary syphilis (sometimes) $
- Viral exanthems (sometimes)

- EM & EDP
- AICTDs & GVHD
- L. sclerosus

BCL

→ perivasc Ly

pig incontinence — Colloid bodies

2- Lichenoid type (lichenoid dermatitis) :

BCL

Lichenoid is defined by the pathologist as a *band-like infiltrate* of inflammatory cells in the superficial dermis. The band of inflammatory cells is usually mostly lymphocytes, except there may be plasma cells (syphilis, inflammation of mucous membranes, Zoon's balanitis) or eosinophils (lichenoid drug reaction). The clinician defines lichenoid differently to mean a papule or plaque resembling a lichen (symbiotic growth of algae and fungi) stuck on the skin. Some diseases that are lichenoid clinically are not lichenoid histologically (e.g. lichen simplex chronicus and lichen spinulosus). Lichen planus is both clinically lichenoid and pathologically lichenoid. Many of the diseases listed below that are histologically lichenoid are not clinically lichenoid.

- LP
- Lichenoid DE
- L. striatus
- L. nitidus
- Lichenoid Keratosis
- Keratosis Lichenoides chronica
- pit. Lichenoides NCPLC
- $ → plasma Cell
- MF → Mg lymphocyte
- Zoon. Balanitis → plasma Cell

30

L.P & Lichenoid Dermatoses

- Called: Classical or Idiopathic L.C

Def. Diseases Resemble L.P Clinically &/or Histopathology.

↓

See classification at Interface Dermatitis.

Lichen planus

- Def. Idiopathic, chronic Inflammatory dis. of (Skin, MM, Hair, Nails) Seen Most Commonly middle
- Pathophysiology:

CMI: Cell mediated immune Response of unknown origin that → damage & basal KCs that express altered self Antigens on their surface.

Some suggested Antigens that may ~~+++~~ the CMI:

1. Viruses: sp.: HCV
2. Vaccines: HBV Vaccines
3. Bacteria: H. pylori (not proved)
4. Contact allergens: amalgam, Copper & Gold
5. Drugs: ACE Inh. "ضغط"

- May be ass. with:
  1. Liver diseases: HCV, HBV, BPC (cirrhosis)
  2. Other Autoimmune dis.: LE, AA, Vitiligo.
  3. Anxiety & depression ± Risk Factor (قلق)

Epidemiology

- Incid.: 1-4% of population.
- Sex & Race: equal
- Age: Any age can be affected but the commonest 30-60 Ys

LP

Classical L.P

Lesion: Papules & plaques:-
- Pruritic
- Polished
- Plentiful
- Purpule
- Planar (Flat Topped)
- Polygonal

→ 8 "Ps" of L.P

Show: Koebner phenomen. / Wickham's stride.

Site: any
- Flexors of wrist.
- dorsal Hands → extensor
- Trunk
- Presacral area
- Medial thighs.
- Shins.
- Glans penis.

Healing → Chic Hyperpigmentation

- NB 1* Wickham's Stride (شريطي زيني / متركسم)

⊙ gray white lace like Network, puncta or lines on the surface of lesions ∈ Can be seen after cleaning the surface of lesion with oil & examination under lens (بالعدسة)
it Represent: the Hypergranulosis seen in L.p"

(بتشوفها اكتر / بتكون واضحة / بتبان اكتر)

Clinical Varieties

Varieties in lesions:
- Linear
- Annular
- Hypertrophic
- Atrophic

Varieties in sites:
- skin (classical) → face, Flexures, PP, Genital
- MM
- Hair
- Nails

- Ulcerative
- Bullous L.p.
- L.p & Bullae (pemphigoides)
- LE/LP overlap synd
- Acute Eruptive ✓ [onset ↔ p]

2* Color Changes seen in L.p:
- initially → erythematous
- later (well developed lesion) → Violaceous
- Old (Resolving lesions) → Hyperpigmented.

3 → Pruritus in L.P

- has a pecular Finding in ☆ there is
  (no) scratch marks & Bloody Crusts
  because most patients React by rubbing
  rather than scratching.
- May precede the appearance of eruptions
  i.e.
+ - it occurs in spasms & cause Frenzied itching
  that lasts For (minutes – hrs.) then gradually ↓

4. Course of L.P disease

- (50%) → Resolve in 9ms.
  (85%) → " " 18ms.
- the Following types tend to be more
  Chronic:
  - Hypertrophic
  - Mucosal (<3% spont. resolution in
  - Annular av. 5yrs).
  - Large lesion
  - childhood type.

Clinical Varities in lesions

⊙ Linear (Zostriform) (1-lor.) may be d.t:
- isolated lesions arranged in lines
- ③ Koebner Phenomenon.
- Following Blaschko lines.

⊙ Annular lesions (10%) Papules dry arranged in Annular pattern.
- d.t either ↗ Papules & plaques Coalesce Central involution
  - Edge: Elevated, purpule – white.
  - Center: hyperpigmented.

NB. usually
- affect: Glans & Flexures.
- (non) itchy
- Chronic.

Hypertrophic (L.p Verrucosus)

- usually at shins & around ankle (tibia)
- very itchy
- very chronic
- very dark post. inflamm. Hyperpigm.

aar: SCC may Arise

DD

(1) Resemble (PS) ?? How to diff ??

- PS
- LSC

- Violaceous
- Very Thick & itchy
- Symmetrical & NO any other Ps. lesions.

(2) (LSC)

Atrophic

- usually represent Resolution of annular or Hypertrophic → (whites)
- Thinned-out plaques (resembling atrophic stage of Morphea or LSA).
- usually at shins.

Ulcerative (Erosive): Rare on skin but Common on:

- MM → oral ulcerative L.p.
- ✓ scalp → CiC. Alopecia.
- Palm & soles → painful ulcers & Erosions
- Vulva + Vagina & gingiva ⟷ "Vulvovaginal gingival synd"
- ✓ Flexual.

Vesicular or Vesiculobullous L.p

(2) clinical Varities

Vesiculobullous L.p

- Bullae affect L.p lesions only
- Seen in: Lower extremities & oral cavity → DIF-ve
- (d.t) Exaggerated subepid space caused by destruction of Basal KCs

فرقين من (BP)

- prognosis better than B.pemphigoides → L.p & Bullae
- L.p Pemphigoides
  - Elm. deposit of IgG at Roof of Bullae. Not Base as BP
  - Bullae develop on Both L.p lesions & NL skin.
  - represent Coexistence of Both L.p & B.Pemphoid
  - DIF +ve → ± L.p + B.P → B.pemphigoides

L.p Erythematosus = LE/Lp overlap synd.

- unusual variant of L.p; ch by Discoid Lesions ē ↗ central atrophy, Hypopigm & Telangiect.
  ↘ periphery: Reddish-Purpule.
- usually at: dorsal Hands & Feet.
- (LE) - (±) ANA
- Path. & DIF: → Features (of) Both: L.p & L.E.
- whether is it L.p (or) L.E ?? unknown
  ∴ search for other L.E manifs.

Dx by (DIF)

(L.p)
- Cytoid staining @ IgG, IgM, C3 at DEJ & intrapid. (↑↑↑)
- shaggy deposit of Fibrinogen (Typical of L.p)

(L.E) linear deposit

• Eruptive L.p (Acute L.p) = Exanthematous

pit. rosea

→ Widely & rapidly Generalized, dissiminated form of L.p:

— Course → self Limited
→ hyperpigm. may ~~x~~ resolve ein (3-4 months) ~~or~~

• Variation in sites of Cut. L.p.

- Face
- Flexures
- pp.
- Genital.

• Flexural L.p (Inverse L.p)

asymptomatic wlc

(1). may be presented (ē) Classical L.p lesions (or) The Hyperpigm ± the sole manifs.

(2) Similar to L.p pigmentosus.

clinical

L.p of The Face = (Actinic L.p = L.p Tropicus)

مكان
- affect sun Exposed areas e.g Face, dorsal Hands, V shapped area of chest.

توقيت
- Start at spring or summer.

شكل
- ch BY: Annular (sometimes Reticulate or diffuse), Hyperpigmented (Blue gray), patche (sometimes plaques) surrounded by rim of Hypopigm.

Type of: With very mild or absent pruritus.

- Pathology: as L.p + Spongiosis (a feature of dermatitis; so some authors Considered it as a variant of photoallergic derma (or PMLE).

NB: Clinical Variants:

1. Classical Type (Dyschromic)
2. Melasma like
3. Granuloma Annulare like [annular]
4. Erythematous: Ass. e CAH & Erosive oral (L.P)

Palmo-plantar L.p

Want to enjoy, other lines ↑↑

← Not as classical lesions of L-p But may be:

1. Firm Papules & Nodules that are surrounded by yellowish hue & may be ass. with spread Thickening of Palms & Soles (Tylosis).

Wart الثؤلول

2. ulcerative Variant ✓ may be ass. with Nail loss sp. Big Toe.

Non Itchy.

Genital L.P

In:

- Male ♂
  - Commonest site: Glans penis
  - Picture: (1) Classical papules, (2) annular pattern, or (3) linear whitish striae
- Female ♀
  - Site: Vulva, Vagina & Anus
  - Picture: (1) whitish macerated lesions, (2) ulcerative

(50%) of ♀ ē oral L.P have undiagnosed Vulvar lesions [2.0 E]

Pathology

(1) Hyperkeratosis (ortho) irreg.
(2) Hyperagranulosis (wicket & irreg. Acanthosis.
(3) Saw toothed Rete < painful
(4) Lichenoid tissue Reaction: →
(5) Flattening rete.

A: خلايا غير حاجبة
- Liquef. degen. B.cl
- Lichenoid infilt. Band like

B: خلايا حاجبة
(Lipsi) ⇐ Colloid Bodies
(ē-) ⇐ Pigment Incontinence (Melanophages)
(ē-) ⇐ Max Joseph spaces (intrabasal)

- DIF. ⇐
  - (A) "Shaggy" deposit of Fibrin at DEJ
  - (B) "g labular" deposits of IgM
  - (C) Cytoid staining of IgG, C3, IgA at DEJ & st. Corneum

L.P of.

- MM (plasma Cell in infilt.) (NB)
- Hair
- Nails.

Mucosal L.P

(1) 3 sites.
(2) 5 associat.
(3) 8 Varities

(سؤال امتحان)

- 3 sites:
  - Oral Cavity: Tongue / buccal mucosa / gingivae / palate
  - Genital: Vulvo Vaginal.
  - others: Tympanic memb. / oesoph / Larynx / Bladder / anus.

Also mar associate cut. L.p but ē Low incid. < oral.

- 5 associations: (Specially ulcerative) (Celiac ± CAH / PBC)
  - HCV
  - DM
  - HTN
  - Mg (مرضى الكلى)
  - Autoimmune diseases: AA, Vitiligo, MG

7 Clinical Varieties of Oral L.P

- Clinical Varieties:
  - Reticular (Commonest): whitish silvery lesions or papules in Reticulate / Linear / annular or Lacelike pattern
  - Pigmented & White plaque like = Leukoplakia
  - Bullous.
  - Atrophic.
  - Erosive [Ulcerative] (1% → SCC)
  - Desquamative: Chr. desquamative gingivitis.
  - Grinspan's Synd.

discomfort & pain ←

Incid. of Isolated oral L.P: 30%
F/M = 1.3 (1) Reticular (2) Erosive (3) depressed Fixed white ple (Leuk. lik

Etiology of oral L.P

- Idiopathic
- Viral: (HCV) HPV, HHV6
- Tooth pastes & Amalgam fillings. ("Contact Allergen")
- oral Lichenoid Drug Eupt^ — Au: Gold; NSAIDs, Antibio.
- Part of GVHD
- Mechanical Trauma.

L.P of the Hair (Follicular L.P = lichen planopilaris)

M(F) 1:4
30–70 Ys
ass. w. Cut & Mucosal in ≥ 50%

4 Varieties:

1. Multiple Follicular Keratotic plug sum. by Violaceous tint
2. Scarring Alopecia & Pseudo pelade of Brocq
3. Graham Little Piccardi-Lassueur Syndrom
   - Triad of:
     - Cic. Alopecia of scalp
     - non Cic. Alopecia of axillae & groin
     - Follicular L.P of Body, scalp or Both.
4. Frontal Fibrosing Alopecia (thought to be L.P variety)
   - unknown cause
   - ± L.P.
   - progressive.
   - post menopausal >50 y.
   - loss of hair of Front & side of scalp
   - skin ± NL / Pale or mildly scarred with Peri follicular redness

L.P of The Nail

Pterygium
→ Pterygium
→ 2o Nail

Varieties:

d.t matrix affection →
- Lat. thining
- Longitudinal ridging – Melanonychia
- Fissuring
- dorsal pterygium → ظفر ظفري

d.t Nail bed affection →
- Yellow discoloration.
- Sub ungual Hyper-Keratosis.
- onycholysis

⊙ Twenty Nail dystrophy syndrome: may occur in children > Adults.

(1) Q What is Pterygium ??

- Pterygium = Greek word means "Wing" ظفري is classically Ass. ب L.P
- Mechanism of its formation: L.P attacks the matrix (Nail forming unit) → permenant destruction & scarring → failure of growth of Nail plate at This site → The proximal Nail fold becomes attached to the Nail bed directly & both grow distally → "Wing" like appearance...

NB
- Pterygium
  - dorsal: L.P, SJS.
  - Ventral: Sclero-derma

- Pterygium inversus ungium: → (scleroderma) Failure of Separation between distal end of Nail Plate & The underlying distal end of The Nail bed.

(2) Q Twenty Nail dystrophy synd (Trachyonychia = Rough)

- Condition Ch BY Progressive Nails affection Call Nail or most Nails
- shows (ridging & pitting & Loss of Luster & roughness)
- usually: at child hood (10-20 y.) 20-25 y → ± improved
- AE: unknown but ± d.t:
  1. L.P
  2. Psoriasis
  3. Eczema
  4. Alopecia A.
  5. Autosomal dominant (AD)
  6. Tr th. ...

Lichenoid Drug Eruptions

(1) Cut. LDE
(2) oral LDE (Lichenoid CD)

ادوية تستخدم لعلاج الورم
مع نقص لوقت تعمل LDE ؟؟
- Griseofulvin
- Flagyl
- Retinoids
- Anti-malarial
- Sulfas.

- These Drugs causes : L.P like lesions (clinically & pathologically)

Lichenoid Drug eruption → "هاجرا"

وكلما كبر العمر (وزاد 12.2 مرة) زادت جرأة ادوية تسبب

Gold is the commonest...
Pattern (1) PR, Eczema, Ps.
(2) Bullous (3) ulcerative
(4) oral (5) Pigmented
(6) Pemphigoides
(7) Erythrod.

1. Anti HTN — ACEI. / BB. / Methyldopa.
2. Antimalarials.
3. Diuretics (chlor & Hydrochlor thiazides)
4. Gold
5. Guinidine.

Lichenoid Drug Eruption. ??

LDE:

Lichenoid CD
(+) oral LDE
Amalgam, Gold, Mercury, Tooth pastes.
Clp as oral L.P

Skin
More:
- Generalized (sparing classical LP sites), larger scaly, itchy, Hyperpigm ↑↑.
- Eczema or Ps. or Pit. Rosea like (Frequently) Photo distributed. (No Wickham's). No hypergranulosis

(No)
- Hair → Severe falling.
- MM → usually spared → (except dental (amalgam Fillings, Gold, Mercury) اطعم الاسنان)

(E)
- Blood : Eosinophilia
- Biopsy → Eosinophilic infiltr. / Parakeratosis
  - Focal interrupt granular layer
  - Cytoid bodies in st. Corneum & granular Layer (rare in LP)
- Hx of Drug intake.
- on stop of drugs → Resolution / Gold Chelators (BAL or EDTA)

14 diuretics → persistent ulceration of Lower Lip

EDP = Ashy dermatosis

- Slowly progressive appearance of gray / gray-blue / gray-brown oval shapped macules & patches at trunk & proxmal extremities ē their axis // to Ribs (as Pit. Rosea) (Follow langers lines)
- Occasionally: may be surr. by peripheral rim of Raised Erythema (may be absent or appear then disappear)

Rim of Raised Erythema

- Clinically: Spare Palms, Soles, mm, Scalp & Nails.
- Prognosis: Children: spont. Resolution: ≃ 70% ē in 2-3 ys
  Adult: more chronic.
- Histopathology: Center of lesion: Post inflammatory Hyperpigm.
  Raised border: Lichenoid React°.
- Treatment: [1] Clofazimine for 3-8 ms
  [2] Laser: for dermal Melanin
  - in children: spont. Resolut° in 70% ē in 2-3 y.
  - Adult → persistent.

NB
- Age ↓
- Oral shape ↓
- Arrangement along langers ↓
- elevated age ±
- distribut°: Neck Trunk & extremit.

IEMP ± variant

Lichen Pigmentosus

- DD from Actinic
  - No classical lesions
  - affect sun-protected areas.

Variant of L.P (Ch BY)

- Affect darker skin individuals III & IV
- Severe hyperpigmentation specially Face / Neck (Face & Flexure)
- May be ass. ē pruritus & L.P lesions elsewhere.
- This type may Represent the usually L.P that Resolve ē marked Hyperpigm (probably d.t the Racial back: ground).

darker skin
Face & Flexure
s.ē

DD EDP: dark skin
Late onset (40-50)
Facial & Flexure

Treatment of L.P (Self Limited ~in 8-18 ms)

Topical (4)

1. Cs
   - Superpotent topical 25gm/w
   - Intralesional (For oral L.P & Hypertrophic L.P)
2. Calcineurine inhibitors (Topical) CI (للوجه)
   - Tacrolimus 0.1% oint
   - Pimecrolimus cream.
3. Cyclosporine (Topical) for ulcerative oral.
4. Retin A Cream (oral L.P).

Systemic (10)

1. Cs
2. MTx
3. Dapsone
4. Cyclosporine
5. Thalidomide
6. Sulfasalazine
7. Mycophenolate Mofetil.
8. Biological
   - Basiliximab
   - Alefacept
   - Efalizumab
   - ← IL2
9. Antimalarial
10. Griseofulvin (حبوب دهنية)
    - Metronidazole
    - Low molecular weight Heparine (LMWH)
11. Retinoids

Phototherapy (6)

- UVA1
- PUVA
- NB-UVB
- Excimer La
- ECP

NB on the

* Topical:
  - Cs: for oral L.P → use Kenalog in Oral base (كريمة عن طريق الفم)
  - Calcineurine: use full in oral L.P & Vulvar lesions (but may ↑ Risk of Mg)
  - Tacrolimus 0.1% oint → Pimicrolimus.

Systemic ttt

Apremilast PDE4 inhibitor
1tor used for ttt of Ps, Rh. arthritis & ank. spondylitis

Cs: indications & systemic Cs

1- Skin L.p < Severe or Acute generalized

2- MM → ulcerative oral L.p

3- Hair → Progressive scarring L.p (Graham little Synd)

4- Nail → Progressive Nail affection.

as: **prednisolone**: 5-20 mg/d for 6ws then gradual withdrawal over 6 ws. (Higher doses are needed in oral Erosive لو كان عندي تقرحات في الفم أو في الجلد)

- Retinoids: **Acitretin** 30 mg/d for 8ws. (Cut) ↓ 50% مرة في اليوم
- MTX: low weekly dose.
- Cyclosporine: for Resistant cases for < Cs & Retinoids
  - useful to ↓↓ progression in Graham Little syn

- Griseofulvin tab: ... لمدة ٢-٤ أشهر [تقرص صباح ، تقرص مساء] يعني
  - ↳ Imperical ttt
  - oral ulcerative لا
  - generalized لا
  - → good Result (but still not universally accepted)
  - → useful in ulcerative oral L.p
- Metronidazole tab: ... ٥٠٠ ملغم يومياً لمدة ١-٢ شهر
  - Immun modulating effect → very good Response in Generalized L.p
- Low Molecular Weight Heparin: (3 mg/kg, S.C) لمرضى الـ Behcet
- Hydroxychloroquine → Excellent in oral L.p. (رأي الدروز)

Graft Versus Host disease or Reaction (GVHD)

def condition That may occur following Transplantat~ in ~~w~~ the donor's Immune Cells in the Transplant (graft) make Antibodies Against the patient Tissues (Host) → Attacking The vital organs.

clp
- Skin → Rash
- GIT → diarrhoea
- Liver → Jaundice.

incid. ① usually following: Hematopoietic stem cell Transplant (HSCT) (90%) → BM

② less common: Solid organ Transplant, Blood Transfusion → immuno-Compromised; Non irradiated To Immuno deficient-Mother-to Immunosuppressed Neonate

Types of GVHR

Acute (< 100 ds) (usually 4-6 wks)

occurs in < 3ms from Transplantation

A. Skin
- 1st: Acral Rash (Foot, Hands & Feet) →
- Then: Generalized maculopapular (Morbilliform) & ± TEN like ± perifollic. Accentuat.

(i) Morbilli f. (ii) Erythrod. (iii) TEN like.

Staging:
- I: Rash < 25% BSA
- II: " 25%-50% "
- III: " 50-100% " (Erythrod)
- IV: Erythroderma & ± bullae / TEN like.

Both types → predispose to skin inf. & Sepsis.

B. GIT → Watery or Bloody diarrhoea & stomach Cramps.

C. Liver → Jaundice & Abn LFTs

3 Mucosa → GIT, liver, eye

Chronic (> 100 ds)

- occurs after > 3ms from Transplantation
- usually evolves from acute but may occur denovo

Skin:
- Early → Lichenoid
- Later → Sclerodermoid
  - LS
  - Morphea form
  - Eosinophilic fasciitis

Mucosa: Eye (KCs), Salivary (Sicca), Bronchiolitis
Exocrine dysf → GIT, pancreas

Tx:
① Hospitalization
② Immunosuppressives: Cs, MTX, CV, Cyclosporin & Tacrolimus

(GVHD) طعم ضد عائل

- MR — Acute : 75٪
  Chr. : 10٪

Clinical staging and histologic grading of acute graft-versus-host disease.

CLINICAL STAGING AND HISTOLOGIC GRADING OF ACUTE GRAFT-VERSUS-HOST DISEASE

	Clinical			Histologic		
Stage	Skin rash	Liver bilirubin	Intestinal tract diarrhea	Grade		
I	<25% BSA	2–3 mg%	500–1000 ml/day	I	Focal or diffuse vacuolar change	→ Vacuol. degen.
2	25–50% BSA	3–6 mg%	1000–1500 ml/day	II	Grade I features + necrosis of keratinocytes and lymphocytes	← Necrosis
3	>50% of BSA – Generalised erythroderma	6–15 mg%	1500–2000 ml/day	III	Grade II features + focal DEJ separation with formation of vesicles	← Vesicles
4	Generalized erythroderma with bulla formation TEN	>15 mg%	Diarrhea, >2000 ml/day Severe abdominal pain, with or without ileus ±	IV	Grade III features + formation of bullae	← Bulae.

HL

Risk of GVHD

(1) Donor
- ↑ Elderly, HLA incompatab.
- Unrelated reciepient
- Male reciepient from ♀

Reciep
- Elderly

3 Stem cell source:
PBC > BM > Cord Blood.

4. More intensive Myeloablat (→ AGVHD) & less aggressive Immunosuppr

DD of AGVHD

(1). Drug Eruption & Viral Exanth.

(2). Engraftment Synd:
- Non specific, in 2 ws
- Fever, Rash, Pulm. Ed.

(3) Toxic Erythema of Chemo Therapy: Specially if PP. or Intertrigenous

** Manifs of Cut

(1) • Combined ē Immunosuppressives:

(2) • Topical Cs (mild dis)

(3) • Phototherapy

(4) • Sun-protect.

Mechanism

(1) AGVHD
- ++ Host APCs ✓
- ++ Donor TCs ✓

(2) CGVHD
- Auto abs product
- Cut. Sclerosis.

** Other Mucocut. Manifs

- Lupus or OM like as SS Photosensitive Erupt
- Xerosis & Ichthyosis
- Leopard like pigm. & vitiligo v depigm.
- KP & poikilod.
- orogenital ulcerat
- Angiomatoid papules
- Hemolytic An.
- Pulm. fibrosis.

HI ✓

- Prophylactic: Cyclosporine, MTX +, Anti-CD52 (Alemtuzumab)
- Active: Cs or others, MM, Sirolimus, Anti-IL2R (daclizumab)

** of Skin

IVIG ← FDA in prevent

Lichen sclerosus

(or Lichen sclerosus et atrophicus)

Def. → Char. inflammatory disorder that affect the skin & mucous memb. & Encompassing 3 disorders:

- Skin → 1- Lichen sclerosus et atrophicus (Ls
- Vulva → 2- Kraurosis Vulvae
- Glans → 3- Balanitis Xerotica obliterans (BXO)

• Epidemiology: ♀ > ♂ (6:1)

• Age: female late → 2 Peaks → Prepubertal (8-13) & Postmenopausal (50-60

• AEt: unknown but ± d.t: (as)

1- Trauma: evidence

. May act as pot. Factor e.g Vaccinat & surgic scar.

. Circumcision → improve it

Pathophysiology

Inflamm. & altered fibroblast funct → Fibrosis

In consider it variant of SCL.

2 Infection: Borrelia Burgdorferi may play a role (±)

3 Autoimmune: • presence of organ specific Abs & Concomitant occurance of other autoimmune diseases.

(Anti glyco-Protein ECM-1).

(2004) → ass. c Histologic evidence of vasculitis → reduplicat of BM.

4 Endocrinal: Evidence

- higher in ♀
- High Incid. Post menopausal & prepubert
- Relation + Menarche

5 Ischemia & Hypoxia → ↑ glut-1 & ↓ VEGF expression in affected skin.

• L.S

- **Genital (85%)**
  - **Male**
    - Balanitis Xerotica obliterans (BXO)
  - **Female**
    - Kraurosis Vulvae
- **Extragenital (15%)**
  - (1) **Cutaneous**
    - A – Usually asymptomatic so
    - B – May be left untreated.
  - (2) **oral MM**
    - Resemble L.P
    - Rare
    - usually: (3) generalize L.S

oral L.S كيترسم حالات الـ
L.P هم كتشخيصها غلط على أنها

Cut. Lichen sclerosus
(LSEA)

CIP:

- **Early Stage:** papules & plaques (Chronic): Guttate – Large
  - White
  - Polygonal
  - Flat topped

  Vitiligo

  Site: Any but Commonly: back / shoulder or.

  - Show: evenly spaced dells or Comedolike Plugs (correspond to obliterated appendageal ostia) & Telangiectasia. (dells of com. / Telang.)
  - Surrounded by Erythematous – Violaceous halo.
  - Size: Few millimeters (Lw like = Guttate) to Large plaques (Entire back like).

- **Late (Atrophic) Stage:**
  - Plugs & dells disappears → White, Soft, Smooth, Wrinkled, Porcelain White plaques.

Symptoms: usually

Genital L.S

(Adults > Children)

SCC

Male

Balanitis Xerotica Obliterans

Sites:

- Commonest → glans & prepuce (inner Aspect)
- Rare: → shaft, scrotum & perineal.

- lesions:
  - Early: → Post Traumatic, Hgic like lesions (bluish Erythematous)
  - Late: white, Atrophic, Sclerotic Plaques → Constriction:
    - phimosis → Failure of retraction of prepuce
    - paraphimosis → ~ ~ Repositioning ~ after retraction
    - Painful Erect⁻ (Dyspareunia)
    - dysuria
    - urinary obst.
    - SCC

NB
- It is more Common in Uncircumcised
- Koebner phenomenon: may be present in L.S.

Female

Kraurosis Vulvae

- Site: usually Vulva & Perianal & then involve other areas e.g Labiae, Cilums.
- Lesion:
  - Early → as in men (but more bluish erythematous common); bullae may occur (DD Sexual Abuse)
  - Late: as in men
    - Perivaginal & Perianal encircling lesions are Common → "Figure of 8" Hour glass or butterfly like.
    - Clitoral & Labial affect⁻ & obliterat⁻ is common.

- Symptoms:
  - Itching
  - Fissuring (3)
  - Erosions
  - dysuria
  - dyspareunia (3)
  - discharge
  - loss (2) → Labia minora, clitoris, urethral meatus
  - Leukoplakia (Sol.) → ± SCC

Prognosis ✓

- Acute genital lesions → good.
- chr. & Extra genital ♀ : → Poor.
  genital.

- Histopathology :-

(in non Mucosal)

1. Hyperkeratosis with Follicular plugging [Compact orthokeratosis]
2. Atrophy of st. Malpighii
3. Hydropic degenerat^ of basal cells. (BCL) (Vacuolar Type Int-f. D
4. Upper dermis : marked Edema & Homogenizat^ of Collagen.
   ↓ sclerosis
5. Mid dermis : → Inflammatory infiltrate (deep band like).

if +ve Sq. Hyperplasia → ± SCC.

- DD : Cut. lesions :
  - ⊙ Morphea.
  - ⊙ Atrophic L.P.
- Genital lesions :
  - Genital L.P
  - LSC
  - VIN
  - Extramammary Pagets. (EMPD)
  - Pemphigoid of MM.

Treatment of LS

CS → Antiinflam immunosuppr (lymphocytes)

- Topical
  - Clearance phase (6-12 ws) Superpotent or ILCs + Tacrolimus
  - Maint. phase ... weekly ... 10 ...
  - CSs (ws) ...
  - Superpotent.
  - CS : Topical & IL
  - Tacrolimus
  - Tretinoin
  - Calcipotriol
  - Emollients.
- Cut
  - ♂ → Circumcision improves it
  - ♀ → (No) excision except if (SCC)
  - Potaba - PDT
  - Reassurance → (No) ne... Fertil...
  - Symptomatic.
  - Potaba | Antimal. arial.
  - PUVA orva, | PDT
  - Acitretin

Potassium - Aminobenzoate = potaba

- one of (Vit B) Members
- Mechanism: Antifibratic & Anti-inflammatory.
  - ↑ Tissue O2 level → ↑ MAO level → -- fibrosis.
- Dose: 12 gm/d (Capsule Potaba = 0.5gm) → divided over 4 doses → gradually to 24 gm/d
  (with meal)
  ٦ع / ٤ جرامات يومياً
- SE: [GIT Upset, Rash] [Hypotension (↓BP), Leukopenia.
- C.I: - sulfonamides
  - Hypoglycemia
  - Renal - dis.

NB: Topical Testosterone is no More effective than Emollient & in one trial was worse than Emollients as maintenance H after clearing ē Cs

NB → Emollient > Topical T

Lichen Nitidus (L.N)

* **Def:** rare, chr., skin Eruption ch by Eruption of
  Micropapules (pin head sized) → Asympt / skin colored / Flat Topped
  usually affect → Children & Young Adults.

* **Aet:** unKnown; Controversy Coexist
  bet. relation of L.P & L-N (Both may Coexist)

* **Epid:** · Sex: M = F
  · Age: any but Commonest → Children / Early Adulthood

* **CIP:**
  Micropapules (1-3 mm) (Pin head sized) (Tend To cluster)
  - Asympt → C but (±) Pruritus)
  - skin Colored (shiny) → (±) (Hyperpigm in blacks)
  - Flat topped → (±) ē central depression)
  - Polygonal or Round → (±) ē Pink-blu-yellow hue)

  Show → Koebner phenomenon → linear Pattern

  Site: L.N may affect:

  A. **Skin:**
  - Commonest → Trunk (Chest & Abd). / Flexor of Upper Extremities / dorsal Hands / genitalia
  - lessCommon: Face, PP., Lower limbs.

  less → B. **MM** → White papules (or) plaques
  less → C. **Nail** → Pitting, ridging, splitting & linear striation. & ± Perungual Lesions.

- Clinical Varieties: [localized / Generalized] [linear / Actinic] [Perforating / Vesicular / Purpuric / Hyic / Keratodermic]

- Prognosis: Spontaneous Resolut^ occurs in (2/3) of cases ≅ in ≤ 1 Y.

- HP: (1) Lichenoid ID
  (2) Infilt. is: Granulomatous
  Hyged by downward prolif. of Rete Ridges (Rek Ridges) « Clutched : Ball & Claw configurat^ of infiltrat^ (2-3 DP width)

- DD: [LP / Fractional Lichenoid dermatitis (Elbow & Knee) / papular ECZ.]
  [papular Sarcoidosis. / L.P / lichen. Scrofluro sorum.]

سؤال امتحان

	LP	Lichen-nitidus.
• Lesion:	• Itchy • Violaceous • pinhead-large sized • PI. Hyperpigm.	• Asympt. • Skin-Colored • Pinhead sized. • Commonly PI. Hypopigm.
⊙ MM ⊙ Hair ⊙ Nails ⊙ Wickham Striae	+Ve	• (Rare) - Absent. X
• (HP)	نفس LP	نفس LP
• TTT	نفس LP	

⊙ (Reassurance) (Self limiting)
• Antihistamines
Imperical ttt • Cs • phototherapy • Acit.
→ Itraconazole.

Lichen Striatus

- Def: Asymptomatic, self limiting, linear dermatosis primarily affect children. (5-15 ys)
- Epid.
  - M:F = 1:2-4
  - Age: 5-15 Ys (rare in infants & Adults)
- Etiology ?? Genetic, Enviramental, AD Autoimmune & viral.
- C/P — Skin: Early stage & Late post. inflamm. stage.
  - Nail
  - ① → Band of Papules (± Vesicles); Scaly, Skin Colored - Erythematous Continous or Interrupted.
    - usually at Single at L-L but
    - ± Bilat at Blaschko at Any site.
  - ② → linear or Blaschkoid Hypopigmented streak
    - ± the 1st presentation] .Ipfs
  - Limb ← Trunk ← ينزل لحد جسم
  - → Self limiting: ē in 3-12 ms → PI- Hypopigm.
  - Nail: ridging, splitting, Subung. Hyperk. onycholysis, dystrophy usually affect the* lat edge of one Nail. ← جسم كيل جس-سد أو الشاي وكيل.
- Investigations ① Dermoscopic:-
  - White structures: Well defined, deep white resembling Wickham striae.
  - Brown structures: Brown, Ketatotic, Cribriform ē red dots surr. by Pale Halo.
- ② HP: lichenoid Type ID, infilt. ch. By ± Granulomatous, Concentrated around HF, Sweat glands
  - Feature of (ECZ+L.P)
  - Epid: Spongiosis, Dysk, Parak.

Linear lesions :-

- VEN
- ILVEN
- Nevoid ps. (linear ps).
- Blaschkitis. (Multiple lines, Trunk, Eczematous)
- Linear: L.P, Darier (HP), GVHD.
- Basal Cell Nevus Synd.
- Basaloid Follicular Hamartoma
- linear porokeratosis (HP)

متشابهين هدا

TTT :-

- Reassurance (Self limiting ein 3-12m)
- Topical Cs
- Emollients
- Pimecrolimus
- Cs + Retinoids

A. Lichen Striatus (Vs) Linear L.P

- Asympt., Erythem. atous → leave → PI Hypopigm
- Severely itchy, Violaceous → leave → PI. Hyperpigm.

B. VEN (Vs) ILVEN

VEN:
- No Erythema
- No Itching
- at birth or Infancy.

ILVEN:
- Erythema
- Marked Itching
- Infancy or childhood.

C. ILVEN (Vs) Linear (Nevoid) PS

ILVEN:
- Early onset/Slowly progressive
- Severely itchy
- (-Ve) Auspitz
- Resistant to ++
- (HP) Psoriasiform + alternating bands of Hypergranulosis (&) overlying orthokeratosis (&) Agranulosis (&) parakeratotic Hypergranulosis.
- Immunohistochi: ↑ K10, ↓ T Cell Substance
- Criteria for ... (No) post inflam hypopig

Linear (Nevoid) PS:
- Late, Slowly Prog.
- Asympt.
- +Ve Auspitz
- Responsive (Sp → Anthralin & Anti TNF).
- (HP) → معروف (PS)
- dermovit under occlusion 3W → dramatic Response
- (No) itching.

Keratosis Lichenoides Chronica

(Nekam's disease)

→ (Rare) Cut. dis start at birth or adulthood (20-40%)
& ch By:

1. Violaceous Keratotic Lichenoid papules
   - Linear & Reticulate or
   - Symmetrical distributed on Limbs &
   - Asymptomatic (↔ L.P) Trunk.
2. S.D. or Rosacea like or psoriasiform Eruption on upper Portion of (Face)
3. Hoarseness of voice & Nail changes, oral ulcers (50%)
4. PPK.

- Course: usually Chronic & may regress (lesions) with Summer & with Aging.
- Histopath: → very similar To (L-P) (may be Considered as a variant of L-P).
- Treatment (symptomatic & unsatisfactory):
  - Cs
  - MTX
  - Cyclosporine
  - Etretinate / ACit. & PUVA or RePUVA
  - Vit A
  - PUVA

DD. HP for (L-P)

- Parakeratosis
- Atrophy of St. Malpighii.

Non itchy L.p

- Annular L.p
- oral
- Hair
- MM
- Nail
- Palmoplanter (pp)
- Actinic L.p